```
LOGINID:Trying 3106016892...Open
ssspta1636axo
Welcome to STN International!  Enter x:
STNLOGON timed out

Trying 3106016892...Open

Welcome to STN International!  Enter x:x
LOGINID:ssspta1636axo
PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2


* * * * * * * * * *   Welcome to STN International   * * * * * * * * * *

 NEWS  1   Feb  2  Web Page URLs for STN Seminar Schedule - N. America
 NEWS  2   Dec 17  Expanded CAplus Coverage of US, Japanese, WIPO,
                   EPO, and German patents
 NEWS  3   Feb  1  Addition of Machine-Translated Abstracts to CAplus
 NEWS  4   Feb  2  STEREO BOND SEARCH PROBLEM FIXED WITH STN EXPRESS 5.0C
 NEWS  5   Feb 14  Homology Searching for Nucleotide Sequences in DGENE
                   now available!
 NEWS  6   Feb 16  BIOTECHNOBASE NOW ON STN
 NEWS  7   Feb 22  New Database Producer Clusters Now Available on STN
 NEWS  8   Feb 28  Structure Search Limits Increased in REGISTRY,
                   ZREGISTRY, and CASREACT
 NEWS  9   Feb 28  Patent Information Now Searchable in CAOLD
 NEWS 10   Mar  1  New IMSDIRECTORY Provides Pharma Company Details
 NEWS 11   Mar 20  INPADOC: PRODUCER WARNING ABOUT DATA DELAYS
 NEWS 12   Mar 22  NEW FEATURES IN INPADOC - RANGE SEARCHING AND NEW
                   SDI/UPDATE SEARCH FIELD

 NEWS EXPRESS  FREE UPGRADE 5.0C NOW AVAILABLE
 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
 NEWS INTER    General Internet Information
 NEWS LOGIN    Welcome Banner and News Items
 NEWS PHONE    Direct Dial and Telecommunication Network Access to STN
 NEWS WWW      CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that
specific topic.

  All use of STN is subject to the provisions of the STN Customer
  agreement.  Please note that this agreement limits use to scientific
  research.  Use for software development or design or implementation
  of commercial gateways or other similar uses is prohibited and may
  result in loss of user privileges and other penalties.

* * * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 16:50:01 ON 03 APR 2000

=> file medline, biosis

COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.15       0.15

FILE 'MEDLINE' ENTERED AT 16:50:11 ON 03 APR 2000

FILE 'BIOSIS' ENTERED AT 16:50:11 ON 03 APR 2000
COPYRIGHT (C) 2000 BIOSIS(R)

=> s temperature and sensitive

L1        40219 TEMPERATURE AND SENSITIVE
```

L5 137945 PROMOTER

=> s l4 and l5

L6 40 L4 AND L5

=> duplicate remove

ENTER L# LIST OR (END):l6

DUPLICATE PREFERENCE IS 'MEDLINE, BIOSIS'
KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):n

PROCESSING COMPLETED FOR L6
L7 26 DUPLICATE REMOVE L6 (14 DUPLICATES REMOVED)

=> d bib ab l7 1-26

L7 ANSWER 1 OF 26 MEDLINE
AN 2000063188 MEDLINE
DN 20063188
TI Essential function of the polo box of Cdc5 in subcellular localization and
induction of cytokinetic structures.
AU Song S; Grenfell T Z; Garfield S; Erikson R L; Lee K S
CS Laboratory of Metabolism, Division of Basic Sciences, National Cancer Institute, National Institutes of Health, Bethesda, Maryland 20892, USA.
NC CA42580 (NCI)
SO MOLECULAR AND CELLULAR BIOLOGY, (2000 Jan) 20 (1) 286-98.
Journal code: NGY. ISSN: 0270-7306.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200003
EW 20000303
AB Members of the polo subfamily of protein kinases play pivotal roles in cell proliferation. In addition to the kinase domain, polo kinases have a strikingly conserved sequence in the noncatalytic C-terminal domain, termed the polo box. Here we show that the budding-**yeast** polo kinase Cdc5, when fused to green fluorescent protein and expressed under its endogenous **promoter**, localizes at spindle poles and the mother bud neck. Overexpression of Cdc5 can induce a class of cells with abnormally elongated buds in a polo box- and kinase activity-dependent manner. In addition to localizing at the spindle poles and cytokinetic neck filaments, Cdc5 induces and localizes to additional septin ring structures within the elongated buds. Without impairing kinase activity, conservative mutations in the polo box abolish the ability of Cdc5 to functionally complement the defect associated with a cdc5-1 **temperature-sensitive** mutation, to localize to the spindle poles and cytokinetic neck filaments, and to induce elongated cells with ectopic septin ring structures. Consistent with the polo box-dependent subcellular localization, the C-terminal domain of Cdc5, but not its polo box mutant, is sufficient for subcellular localization, and its overexpression appears to inhibit cytokinesis. These data provide evidence that the polo box is required to direct Cdc5 to specific subcellular locations and induce or organize cytokinetic structures.

L7 ANSWER 2 OF 26 MEDLINE
AN 1999412354 MEDLINE
DN 99412354
TI Casein kinase 2-mediated phosphorylation of respiratory syncytial virus phosphoprotein P is essential for the transcription elongation activity of the viral polymerase; phosphorylation by casein kinase 1 occurs mainly at Ser(215) and is without effect.
AU Dupuy L C; Dobson S; Bitko V; Barik S
CS Department of Biochemistry and Molecular Biology, College of Medicine, University of South Alabama, Mobile, Alabama, USA.
NC AI37938 (NIAID)

protein or in the presence of phosphate-free P protein produced abortive initiation product[redacted]ut no full-length transcripts. [redacted]recombinant P protein in which Se[redacted](232) was mutated to Asp exhibit[redacted] about half of the transcriptional activity of the wild-type phosphorylated protein, suggesting that the negative charge of the phosphate groups is an important contributor to P protein function. Use of a **temperature -sensitive** CK2 mutant **yeast** revealed that in **yeast**, phosphorylation of recombinant P by non-CK2 kinase(s) occurs mainly at Ser(215). In vitro, P protein could be phosphorylated by purified CK1 at Ser(215) but this phosphorylation did not result in transcriptionally active P protein. A triple mutant P protein in which Ser(215), Ser(232), and Ser(237) were all mutated to Ala was completely defective in phosphorylation in vitro as well as ex vivo. The xanthate compound D609 inhibited CK2 but not CK1 in vitro and had a very modest effect on P protein phosphorylation and RSV yield ex vivo. Together, these results suggest a role for CK2-mediated phosphorylation of the P protein in the **promoter** clearance and elongation properties of the viral RNA-dependent RNA polymerase.

L7 ANSWER 3 OF 26 MEDLINE
AN 1999418886 MEDLINE
DN 99418886
TI A transmembrane hybrid-type histidine kinase in Arabidopsis functions as an osmosensor.
AU Urao T; Yakubov B; Satoh R; Yamaguchi-Shinozaki K; Seki M; Hirayama T; Shinozaki K
CS Biological Resources Division, Japan International Research Center for Agricultural Science (JIRCAS), Ministry of Agriculture, Forestry and Fisheries, 1-2 Oowashi, Tsukuba, Ibaraki 305, Japan.
SO PLANT CELL, (1999 Sep) 11 (9) 1743-54.
Journal code: BJU. ISSN: 1040-4651.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200003
EW 20000304
AB Water deficit and the resulting osmotic stress affect plant growth. To understand how plant cells monitor and respond to osmotic change from water stress, we isolated a cDNA from dehydrated Arabidopsis plants. This cDNA encodes a novel hybrid-type histidine kinase, ATHK1. Restriction fragment length polymorphism mapping showed that the ATHK1 gene is on chromosome 2. The predicted ATHK1 protein has two putative transmembrane regions in the N-terminal half and has structural similarity to the **yeast** osmosensor synthetic lethal of N-end rule 1 (SLN1). The ATHK1 transcript was more abundant in roots than other tissues under normal growth conditions and accumulated under conditions of high or low osmolarity. Histochemical analysis of beta-glucuronidase activities driven by the ATHK1 **promoter** further indicates that the ATHK1 gene is transcriptionally upregulated in response to changes in external osmolarity. Overexpression of the ATHK1 cDNA suppressed the lethality of the **temperature-sensitive** osmosensing-defective **yeast** mutant sln1-ts. By contrast, ATHK1 cDNAs in which conserved His or Asp residues had been substituted failed to complement the sln1-ts mutant, indicating that ATHK1 functions as a histidine kinase. Introduction of the ATHK1 cDNA into the **yeast** double mutant sln1Delta sho1Delta, which lacks two osmosensors, suppressed lethality in high-salinity media and activated the high-osmolarity glycerol response 1 (HOG1) mitogen-activated protein kinase (MAPK). These results imply that ATHK1 functions as an osmosensor and transmits the stress signal to a downstream MAPK cascade.

L7 ANSWER 4 OF 26 MEDLINE
AN 97286549 MEDLINE
DN 97286549
TI The signal peptidase II (Isp) gene of Bacillus subtilis.
AU Pragai Z; Tjalsma H; Bolhuis A; van Dijl J M; Venema G; Bron S
CS Department of Genetics, University of Groningen, Groningen Biomolecular Sciences and Biotechnology Institute, Haren, The Netherlands.
SO MICROBIOLOGY, (1997 Apr) 143 (Pt 4) 1327-33.
Journal code: BXW. ISSN: 1350-0872

II. The deduced amino acid sequence of the B. subtilis SPase II showed significant similarity with those of other known SPase II enzymes. Activity of the B. subtilis SPase II was demonstrated by a pulse-labelling experiment in E. coli. In B. subtilis, the Isp gene is flanked by the isoleucyl-tRNA synthetase (ileS) gene and the pyrimidine biosynthetic (pyr) gene cluster, which is known to map at 139 degrees of the chromosome. In the Gram-positive bacteria studied thus far, Isp appears to be the first gene in an operon. The **promoter**-distal gene ("orf4') of this operon specifies a hypothetical protein in bacteria and **yeast**.

L7 ANSWER 5 OF 26 MEDLINE DUPLICATE 1
AN 97178386 MEDLINE
DN 97178386
TI Complementation of **temperature-sensitive** topoisomerase II mutations in Saccharomyces cerevisiae by a human TOP2 beta construct allows the study of topoisomerase II beta inhibitors in **yeast**.
AU Meczes E L; Marsh K L; Fisher L M; Rogers M P; Austin C A
CS Department of Biochemistry and Genetics, Medical School, University of Newcastle-upon-Tyne, U.K.
SO CANCER CHEMOTHERAPY AND PHARMACOLOGY, (1997) 39 (4) 367-75.
Journal code: C9S. ISSN: 0344-5704.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199705
EW 19970501
AB We show herein that human DNA topoisomerase II beta is functional in **yeast**. It can complement a **yeast temperature-sensitive** mutation in topoisomerase II. The effect on human topoisomerase II beta of a number of topoisomerase II inhibitors was analysed in a **yeast** in vivo system and compared with that of human topoisomerase II alpha and wild-type **yeast** topoisomerase II. A drug permeable **yeast** strain (JN394 top2-4) was used to analyse the in vivo effects of known anti-topoisomerase II agents on human topoisomerase II beta transformants. A parallel analysis on human topoisomerase II alpha transformants provides the first in vivo analysis of the responses of **yeast** bearing the individual isoforms to these drugs. The strain was analysed at **35** degrees C, a non-permissive **temperature** at which only plasmid-borne topoisomerase II is active. A shuttle vector with either human topoisomerase II beta, human topoisomerase II alpha or **yeast** topoisomerase II under the control of a GAL1 **promoter** was used. The key findings were that amsacrine produced comparable levels of cell killing with both alpha and beta, whilst etoposide, doxorubicin and mitoxantrone produced higher degrees of cell killing with alpha than with beta or **yeast** topoisomerase II. Merbarone had the greatest effect on the **yeast** strain bearing plasmid-borne **yeast** topoisomerase II. Suramin, quercetin and genistein showed little cell killing in this system. This **yeast** in vivo system provides a powerful way to analyse the effects of anti-topoisomerase II agents on transformants bearing the individual human isoforms. This system also provides a means of analysing putative drug-resistance mutations in human topoisomerase II beta or to select for drug-resistance mutations in human topoisomerase II beta.

L7 ANSWER 6 OF 26 MEDLINE DUPLICATE 2
AN 97293233 MEDLINE
DN 97293233
TI Molecular cloning and expression of the Candida albicans TOP2 gene allows study of fungal DNA topoisomerase II inhibitors in **yeast**.
AU Keller B A; Patel S; Fisher L M
CS Molecular Genetics Group, Department of Cellular and Molecular Sciences, St. George's Hospital Medical School, University of London, Cranmer Terrace, London SW17 0RE, U.K.
SO BIOCHEMICAL JOURNAL, (1997 May 15) 324 (Pt 1) 329-39.
Journal code: 9YO. ISSN: 0264-6021.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)

fragment that mapped to chromosome 4. It was used to construct a plasmid in which TOP2 expresses a recombinant enzyme (residues 57-1461 of C. albicans topoisomerase II fused to the first five residues of Saccharomyces cerevisiae topoisomerase II) under the control of a galactose-inducible **promoter**. The plasmid rescued the lethal phenotype of a **temperature-sensitive** S. cerevisiae DNA topoisomerase II mutant allowing growth at **35** degrees C. **Yeast** cells, bearing ISE2 permeability and rad52 double-strand-break-repair mutations the growth of which at **35** degrees C was dependent on C. albicans topoisomerase II, were killed by the known topoisomerase II inhibitors amsacrine and doxorubicin. Parallel experiments in **yeast** expressing human topoisomerase IIalpha allowed the relative sensitivities of the fungal and host topoisomerases to be examined in the same genetic background. To compare the killing in vivo with drug inhibition in vitro, the recombinant C. albicans topoisomerase II protein was expressed and purified to near-homogeneity from S. cerevisiae yielding a 160 kDa polypeptide that displayed the expected ATP-dependent DNA-relaxation and DNA-decatenation activities. The enzyme, whether examined in vitro or complementing in S. cerevisiae, was comparably **sensitive** to amsacrine and doxorubicin. Our results suggest that potential topoisomerase II-targeting anti-fungal inhibitors can be identified and studied in S. cerevisiae.

L7 ANSWER 7 OF 26 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1997:456399 BIOSIS
DN PREV199799755602
TI Screening the p53 status of human cell lines using a **yeast** functional assay.
AU Jia, Li-Qun; Osada, Motonobu; Ishioka, Chikashi (1); Gamo, Makio; Ikawa, Shuntao; Suzuki, Takao; Shimodaira, Hideki; Niitani, Tomohito; Kudo, Toshio; Akiyama, Mitoshi; Kimura, Narimiti; Matsuo, Mitsuyoshi; Mizusawa, Hiroshi; Tanaka, Noriho; Koyama, Hideki; Namba, Masayoshi; Kanamaru, Ryunosuke; Kuroki, Toshio
CS (1) Inst. Dev. Aging Cancer, Tohoku University, 4-1 Seiryo-machi, Aoba-ku, Sendai 980 Japan
SO Molecular Carcinogenesis, (1997) Vol. 19, No. 4, pp. 243-253. ISSN: 0899-1987.
DT Article
LA English
AB We have screened the p53 status of 156 human cell lines, including 142 tumor cell lines from 27 different tumor types and 14 cell lines from normal tissues by using functional analysis of separated alleles in **yeast**. This assay enables us to score wild-type p53 expression on the basis of the ability of expressed p53 to transactivate the reporter gene HIS3 via the p53-responsive GAL1 **promoter** in Saccharomyces cerevisiae. Of 142 tumor cell lines, at least 104 lines (73.2%) were found to express the mutated p53 gene: 94 lines (66.2%) were mutated in both alleles, three lines (2.1%) were heterozygous, and no p53 cDNA was amplified from seven lines (4.9%). Of the 14 cell lines originating from normal tissues, all the transformed or immortalized cell lines expressed mutant p53 only. **Yeast** cells expressing mutant p53 derived from 94 cell lines were analyzed for **temperature-sensitive** growth.p53 cDNA from eight cell lines showed p53-dependent-**temperature-sensitive** growth, growing at 30 degree C but not at **37** degree C. Four **temperature-sensitive** p53 mutations were isolated: CAT fwdarw CGT at codon 214 (H214R), TAC fwdarw TGC at codon 234 (Y234C), GTG fwdarw ATG at codon 272 (V272M), and GAG fwdarw AAG (E285K). Functionally wild-type p53 was detected in 38 tumor cell lines (26.8%) and all of the diploid fibroblasts at early and late population doubling levels. These results strongly support the previous findings that p53 inactivation is one of the most frequent genetic events that occurs during carcinogenesis and immortalization.

L7 ANSWER 8 OF 26 MEDLINE DUPLICATE 3
AN 96210557 MEDLINE
DN 96210557
TI Membrane lipid perturbation modifies the set point of the **temperature** of heat shock response in **yeast**.
AU Carrat`u L; Franceschelli S; Pardini C L; Kobayashi G S; Horvath I; Vigh L; Maresca B

AB Addition of a saturated fatty acid (SFA) induced a strong increase in heat shock (HS) mRNA transcription when cells were heat-shocked at **37** degrees C, whereas treatment with an unsaturated fatty acid (UFA) reduced or eliminated the level of HS gene transcription at **37** degrees C. Transcription of the delta 9-desaturase gene (Ole1) of Histoplasma capsulatum, whose gene product is responsible for the synthesis of UFA, is up-regulated in a **temperature-sensitive** strain. We show that when the L8-14C mutant of Saccharomyces cerevisiae, which has a disrupted Ole1 gene, is complemented with its own Ole1 coding region under control of its own **promoter** or Ole1 promoters of H. capsulatum, the level of HS gene transcription depends on the activity of the promoters. Fluorescence anisotropy of mitochondrial membranes of completed strains corresponded to the different activity of the Ole1 **promoter** used. We propose that the SFA/UFA ratio and perturbation of membrane lipoprotein complexes are involved in the perception of rapid **temperature** changes and under HS conditions disturbance of the preexisting membrane physical state causes transduction of a signal that induces transcription of HS genes.

L7 ANSWER 9 OF 26 MEDLINE DUPLICATE 4
AN 97093966 MEDLINE
DN 97093966
TI Highly conserved toxicity of Saccharomyces cerevisiae Rap1p.
AU Chambers A
CS Department of Genetics, University of Nottingham, Queen's Medical Centre, UK.. Alistair.Chambers@nottingham.ac.uk
SO MOLECULAR MICROBIOLOGY, (1996 Nov) 22 (3) 449-58.
Journal code: MOM. ISSN: 0950-382X.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199705
EW 19970503
AB Budding **yeast** (Saccharomyces cerevisiae) Rap1p has been expressed in fission **yeast** (Schizosaccharomyces pombe) under the control of the regulatable fructose bisphosphatase (fbp) **promoter**. When the fbp **promoter** was derepressed, cells containing the complete RAP1 gene failed to show any significant growth, suggesting that Rap1p is toxic. A derivative of Rap1p that has a **temperature-sensitive** mutation in the DNA-binding domain was not toxic in cells grown at **37** degrees C, a **temperature** at which DNA binding by rap1p(ts) is severely inhibited. Removal of a short region downstream of the DNA-binding domain, including a region previously shown to be essential for Rap1p toxicity in budding **yeast**, also abolished the toxic effect. The toxic effect of Rap1p has therefore been conserved between two distantly related yeasts. In budding **yeast**, overexpression of Rap1p also caused changes to the lengths of the telomeric repeats. No effects on telomeres were detected in fission **yeast**.

L7 ANSWER 10 OF 26 MEDLINE DUPLICATE 5
AN 96242146 MEDLINE
DN 96242146
TI A multicopy suppressor of nin1-1 of the **yeast** Saccharomyces cerevisiae is a counterpart of the Drosophila melanogaster diphenol oxidase A2 gene, Dox-A2.
AU Kawamura M; Kominami K; Takeuchi J; Toh-e A
CS Department of Biological Sciences, Graduate School of Science, University of Tokyo, Japan.
SO MOLECULAR AND GENERAL GENETICS, (1996 May 23) 251 (2) 146-52.
Journal code: NGP. ISSN: 0026-8925.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199610
AB NIN1 is an essential gene for growth of the **yeast** Saccharomyces

phenotype of a strain deleted for sun2. This Dox-A2-dependent strain was **temperature sensiti** and accumulated dumb-bell-shap cells, with an undi ded nucleus at the isthmus, aft **temperature** upshift. This morphology is similar to that of nin1-1 cells kept at a restrictive **temperature**. These results suggest that SUN2 is a functional counterpart of Dox-A2 and that these genes play a pivotal role in the cell cycle in each organism.

L7 ANSWER 11 OF 26 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1994:269606 BIOSIS
DN PREV199497282606
TI Control of secretory production of human lysozyme from Saccharomyces cerevisiae by incubation **temperature** and phosphate concentration.
AU Hiraoka, Emi; Murai, Masatoshi; Yano, Jyun-Ichi; Bun-Ya, Masanori; Harashima, Satoshi; Oshima, Yasuji (1)
CS (1) Dep. Biotechnol., Fac. Eng., Osaka Univ., 2-1 Yamadaoka, Suita-shi, Osaka 565 Japan
SO Journal of Fermentation and Bioengineering, (1994) Vol. 77, No. 4, pp. 376-381.
ISSN: 0922-338X.
DT Article
LA English
AB A system for the controlled expression of a foreign gene in Saccharomyces cerevisiae by **temperature** and/or inorganic phosphate (P-i) concentration in the medium was constructed. A DNA fragment bearing the **promoter** of the PHO84 gene, which encodes a P-i transporter of S. cerevisiae and is derepressed by P-i starvation, was used as **promoter**. When a cDNA fragment encoding the human lysozyme (h-lysozyme) gene connected with the PHO84 **promoter** was ligated into a YEp vector, a maximum of 4.5 mg/l of the enzyme was secreted from the host cells in low-P-i medium. When a **temperature-sensitive** pho81 mutant was used as the host with this vector, 2.6 mg/l of h-lysozyme was secreted in low-P-i medium at 25 degree C and its production was turned off at **37** degree C.

L7 ANSWER 12 OF 26 MEDLINE DUPLICATE 6
AN 94235223 MEDLINE
DN 94235223
TI Catabolite repression and induction time effects for a **temperature-sensitive** GAL-regulated **yeast** expression system.
AU Napp S J; Da Silva N A
CS Department of Chemical and Biochemical Engineering, University of California, Irvine 92717..
SO JOURNAL OF BIOTECHNOLOGY, (1994 Feb 28) 32 (3) 239-48.
Journal code: AL6. ISSN: 0168-1656.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS B
EM 199408
AB The effects of residual catabolite repression and the importance of induction timing were determined for a **temperature-sensitive** (ts) GAL-regulated stable **yeast** expression system. The Saccharomyces cerevisiae strain employed carries a reg1 mutation inhibiting catabolite repression, and a ts mutation enabling induction of the regulated GAL promoters by a **temperature** shift to **35** degrees C. Despite the reg1 mutation and induction method, glucose depressed lacZ expression from a GAL1 **promoter** during batch culture. beta-Galactosidase specific activity was consistently lower at higher initial glucose concentrations in both SDC (semi-defined) and YPDa (complex) media; decreases of 18-**36**% were observed as glucose concentration was increased between 1, 3, 5, and 10 g l-1. However, the reductions in beta-galactosidase specific activity due to residual catabolite repression were more than balanced by substantial improvements in biomass yield at higher glucose levels. Therefore, productivity rose with increasing glucose concentration; in YPDa medium, increasing initial glucose from 1 to 10 g l-1 resulted in a 2.6-fold increase in beta-galactosidase volumetric activity. Due to the negative effects of shifting **temperature** to **35** degrees C, the trade-offs between optimum growth and a lengthy induction period were also

Osaka, Japan..
SO APPLIED MICROBIOLOGY AND BIOTECHNOLOGY, (1993 Nov) (2-3) 333-40.
Journal code: AMC. ISSN: 0175-7598.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS B
EM 199405
AB We constructed a plasmid that directs the synthesis and secretion of hepatitis B virus (HBV) surface antigen (HBsAg) particles by Saccharomyces cerevisiae. This plasmid contains a proteinase-resistant HBsAg M (M-P31c) gene fused at its 5'-terminus with a chicken-lysozyme signal peptide (C-SIG) gene, which is placed under the **yeast** GLD (glyceraldehyde-3-phosphate dehydrogenase gene) **promoter**. The products encoded by the "C-SIG+M-P31c" (LM-P31c) gene were synthesized and assembled themselves into HBsAg particles in **yeast** cells, and the particles were released into the medium along with poly-HSA (polymerized human serum albumin) binding activity. The HBsAg particles purified from the medium were very similar in density (1.19 g cm-3), size (19.2 +/- 0.8 nm in diameter) and shape (sphere) to human-plasma-derived HBsAg particles. When several sec (**temperature-sensitive** secretion-defective) mutants were used as host cells, the release of HBsAg particles into the medium was blocked at **37** degrees C but not at 25 degrees C, indicating that the HBsAg particles are exported through the normal **yeast** secretion pathway. To our knowledge, this is the first report that **yeast** cells are capable of secreting particles into the medium.

L7 ANSWER 14 OF 26 MEDLINE
AN 93154319 MEDLINE
DN 93154319
TI CDC39, an essential nuclear protein that negatively regulates transcription and differentially affects the constitutive and inducible HIS3 promoters [published erratum appears in EMBO J 1993 Jul;12(7):2990].
AU Collart M A; Struhl K
CS Department of Biological Chemistry and Molecular Pharmacology, Harvard Medical School, Boston, MA 02115..
NC GM30186 (NIGMS)
SO EMBO JOURNAL, (1993 Jan) 12 (1) 177-86.
Journal code: EMB. ISSN: 0261-4189.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-X70151; GENBANK-S57804; GENBANK-L09676; GENBANK-L09677; GENBANK-L09678; GENBANK-L09679; GENBANK-L09680; GENBANK-L09681; GENBANK-L09682; GENBANK-L09683
EM 199305
AB The **yeast** HIS3 **promoter** region contains two functionally distinct TATA elements, TC and TR, that are responsible respectively for initiation from the +1 and +13 sites. Both TC and TR support basal HIS3 transcription and require the TATA binding protein TFIID, but only TR responds to transcriptional activation by GCN4 and GAL4. By selecting for **yeast** strains that increase transcription by a GCN4 derivative with a defective activation domain, we have isolated a **temperature-sensitive** mutation in CDC39, a previously defined gene implicated in cell-cycle control and the pheromone response. This cdc39-2 mutation causes increased basal transcription of many, but not all genes, as well as increased transcriptional activation by GCN4 and GAL4. Surprisingly, basal HIS3 transcription from the +1 initiation site is strongly increased, while initiation from the +13 site is barely affected. Thus, unlike acidic activator proteins that function through TR, CDC39 preferentially affects transcription mediated by TC. CDC39 is an essential gene that encodes a very large nuclear protein (2108 amino acids) containing two glutamine-rich regions. These observations

Journal code: YEA. ISSN: 0749-503X.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-X57629
EM 199306
AB The SCH9 **yeast** gene, that was previously identified as a suppressor of cdc25 and ras1- ras2-ts **temperature-sensitive** mutants, encodes a putative protein kinase that positively regulates the progression of **yeast** cells through the G1 phase of the cell cycle. We have determined the structure of the SCH9 transcription unit, using primer extension and S1 mapping techniques. The corresponding mRNA included an unusually long 5' region of more than 600 nucleotides preceding the major open reading frame (ORF). While the latter corresponded to a protein of 824 amino acids, an upstream open reading frame (uORF) within the 5' leader could potentially encode a 54 amino acid peptide. To investigate the role of the AUGs within the uORF, we engineered chimaeric plasmid vectors in which SCH9 sequences including the **promoter**, the mRNA leader and the first 514 nucleotides of the major ORF were fused in-frame with beta-galactosidase-coding sequences. Upon introduction into **yeast** cells, the fusion protein was efficiently expressed. However, mutational disruption of the uORF using oligonucleotide-directed mutagenesis did not affect the level of expression of the fusion protein. This indicates that regulatory mechanisms in Saccharomyces cerevisiae prevent upstream AUGs within the SCH9 mRNA leader sequence from influencing translation from downstream initiation codons.

L7 ANSWER 16 OF 26 MEDLINE DUPLICATE 8
AN 92253348 MEDLINE
DN 92253348
TI Mammalian p53 can function as a transcription factor in **yeast**.
AU Scharer E; Iggo R
CS Swiss Institute for Experimental Cancer Research, ISREC, Epalinges..
SO NUCLEIC ACIDS RESEARCH, (1992 Apr 11) 20 (7) 1539-45.
Journal code: O8L. ISSN: 0305-1048.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199208
AB p53 has previously been shown to contain a transactivation domain using GAL4 fusion proteins and to bind specifically to a **33** base pair DNA sequence in immunoprecipitation assays. We show here that mammalian p53 expressed in S. cerevisiae is able to activate transcription of a reporter gene placed under the control of a CYC1 hybrid **promoter** containing the **33** base pair p53-binding sequence. The activation is dependent on the orientation and number of copies of the binding site. Three p53 mutants commonly found in human tumours, 175H, 248W and 273H, are unable to activate transcription. A fourth human p53 mutant, 285K, is **temperature-sensitive** for transcriptional activation. Murine p53 activates transcription from the same sequence. The murine 135V mutant, which is **temperature-sensitive** for mammalian cell transformation, is also **temperature-sensitive** for transcriptional activation. There is a much better correlation between mutation and transcriptional competence than between mutation and the structure of p53 determined with conformation-**sensitive** antibodies. We have therefore developed a simple transcription assay for p53 mutation in which **yeast** are transfected with p53 PCR products and mutation is scored on X-gal plates.

L7 ANSWER 17 OF 26 MEDLINE DUPLICATE 9
AN 93046688 MEDLINE
DN 93046688
TI Nucleosome disruption at the **yeast** PHO5 **promoter** upon PHO5 induction occurs in the absence of DNA replication.
AU Schmid A; Fascher K D; Horz W
CS Institute for Physiological Chemistry, Universitat Munchen, Germany.

be activated in the presence of phosphate by a **temperature** shift from 24 degrees C to 37 degrees C. Under these conditions, the **promoter** undergoes the same chromatin transition as in phosphate-starved cells. Disruption of the nucleosomes by the **temperature** shift also occurs when DNA replication is prevented. Nucleosomes re-form when the **temperature** is shifted from 37 degrees C back to 24 degrees C in nondividing cells. Glucose is required for the disruption of the nucleosomes during the **temperature** upshift, not for their re-formation during the **temperature** downshift. These experiments prove that DNA replication is not required for the transition between the nucleosomal and the non-nucleosomal state at the PHO5 **promoter**.

L7 ANSWER 18 OF 26 MEDLINE DUPLICATE 10
AN 91210324 MEDLINE
DN 91210324
TI Expression of the **yeast** plasma membrane [H+]ATPase in secretory vesicles. A new strategy for directed mutagenesis.
AU Nakamoto R K; Rao R; Slayman C W
CS Department of Human Genetics, Yale University School of Medicine, New Haven, Connecticut 06510..
NC GM 15761 (NIGMS)
GM 11146 (NIGMS)
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1991 Apr 25) 266 (12) 7940-9.
Journal code: HIV. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199108
AB Secretory vesicles that accumulate in the **temperature-sensitive** sec6-4 strain of **yeast** have been shown to contain a vanadate-**sensitive** ATPase, presumably en route to the plasma membrane (Walworth, N. C., and Novick, P. J. (1987) J. Cell Biol. 105, 163-174). We have now established this enzyme to be a fully functional form of the PMA1 [H+]ATPase, identical in its catalytic properties to that found in the plasma membrane. In addition, the secretory vesicles are sealed tightly enough to permit the measurement of ATP-dependent proton pumping with fluorescent probes. We have gone on to exploit the vesicles as an expression system for site-directed mutants of the ATPase. For this purpose, a sec6-4 strain has been constructed in which the chromosomal PMA1 gene is under control of the GAL1 **promoter**; the mutant pma1 allele to be studied is introduced on a centromeric plasmid under the control of a novel heat shock **promoter**. In galactose medium at 23 degrees C, the wild-type ATPase is produced and supports normal vegetative growth. When the cells are switched to glucose medium at 37 degrees C, however, the wild-type gene turns off, the mutant gene turns on, and secretory vesicles accumulate. The vesicles contain a substantial amount of newly synthesized, plasmid-encoded ATPase (5-10% of total vesicle protein), but only traces of residual wild-type PMA1 ATPase and no detectable mitochondrial ATPase, vacuolar ATPase, or acid or alkaline phosphatase. To test the expression strategy, we have made use of pma1-105 (Ser368----Phe), a vanadate-resistant mutant previously characterized by standard methods (Perlin, D. S., Harris, S. L., Seto-Young, D., and Haber, J. E. (1989) J. Biol. Chem. 264, 21857-21864). In secretory vesicles, as expected, the plasmid-borne pma1-105 allele gives rise to a mutant enzyme with a reduced rate of ATP hydrolysis and a 100-fold increase in Ki for vanadate. Proton pumping is similarly resistant to vanadate. Thus, the vesicles appear well suited for the production and characterization of mutant forms of the PMA1 [H+]ATPase. They should also aid the study of other **yeast** membrane proteins that are essential for growth as well as heterologous proteins whose appearance in the plasma membrane may be toxic to the cell.

L7 ANSWER 19 OF 26 MEDLINE DUPLICATE 11
AN 91334390 MEDLINE
DN 91334390

AB The RNA subunit of Saccharomyces cerevisiae nuclear RNase P is encoded by a single-copy, essential gene, RPR1. The 369-nucleotide mature form of the RNA has an apparent precursor with an 84-nucleotide 5' leader and approximately **33** nucleotides of additional 3' sequence. Analysis of RPR1 transcription in a strain with a **temperature-sensitive** lesion in RNA polymerase III shows that the gene is transcribed in vivo by RNA polymerase III. Examination of potential **promoter** regions using both progressive upstream deletions and point mutations indicates that at least two sequences contained within the 5' leader region are essential for expression in vivo, while sequences farther upstream influence efficiency. The required leader elements resemble tRNA gene-like A-box and B-box internal promoters in sequence and spacing. As in the tRNA genes, transcription factor TFIIIC binds to this region in vitro and binding is severely reduced by either A-box or B-box point mutations that impair expression in vivo. It thus appears that the **yeast** RNase P RNA gene has adopted a **promoter** strategy that places an RNA polymerase III "internal" **promoter** upstream of the mature structural domain to help drive transcription.

L7 ANSWER 20 OF 26 MEDLINE
AN 91088271 MEDLINE
DN 91088271
TI Increased dosage of the MSN1 gene restores invertase expression in **yeast** mutants defective in the SNF1 protein kinase.
AU Estruch F; Carlson M
CS Department of Genetics, Columbia University College of Physicians and Surgeons, New York, 10032..
NC GM34095 (NIGMS)
SO NUCLEIC ACIDS RESEARCH, (1990 Dec 11) 18 (23) 6959-64.
Journal code: O8L. ISSN: 0305-1048.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
OS GENBANK-X54324
EM 199104
AB The SNF1 protein kinase is required for expression of the invertase gene in response to glucose deprivation in Saccharomyces cerevisiae. We selected for genes that in multicopy suppress the invertase defect of **temperature-sensitive** snf1 mutants. Increased dosage of the MSN1 gene restores high-level, regulated invertase expression in snf1-ts mutants, and disruption of MSN1 in the wild type reduces invertase expression a fewfold. MSN1 gene dosage does not affect SNF1 protein kinase activity in vitro. MSN1 encodes a 43-kilodalton protein, and a MSN1-beta-galactosidase fusion protein was localized in the nucleus. A LexA-MSN1 fusion protein, when bound to a lexA operator, activates transcription of an adjacent **promoter**. In vitro synthesized MSN1 protein exhibits weak, nonspecific DNA-binding activity.

L7 ANSWER 21 OF 26 MEDLINE
AN 90349597 MEDLINE
DN 90349597
TI DNA metabolism gene CDC7 from **yeast** encodes a serine (threonine) protein kinase.
AU Hollingsworth R E Jr; Sclafani R A
CS Department of Biochemistry, Biophysics, and Genetics, University of Colorado Health Sciences Center, Denver 80262.
NC GM35078 (NIGMS)
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1990 Aug) 87 (16) 6272-6.
Journal code: PV3. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199011
AB The **yeast** Cdc7 protein is indispensable to initiation of nuclear

Cdc7 may regulate the various DNA metabolic pathways by phosphorylating one or more target substrates. Because Cdc7 kinase acts downstream of Cdc28/cdc2 kinase function at "start," the transition from G1 to S phase in the cell cycle may be the result of a cascade of protein phosphorylation.

L7 ANSWER 22 OF 26 MEDLINE DUPLICATE 12
AN 90269231 MEDLINE
DN 90269231
TI The ryh1 gene in the fission **yeast** Schizosaccharomyces pombe encoding a GTP-binding protein related to ras, rho and ypt: structure, expression and identification of its human homologue.
AU Hengst L; Lehmeier T; Gallwitz D
CS Max-Planck-Institute for Biophysical Chemistry, Department of Molecular Genetics, Gottingen, FRG.
SO EMBO JOURNAL, (1990 Jun) 9 (6) 1949-55.
Journal code: EMB. ISSN: 0261-4189.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-X52475
EM 199009
AB A gene, ryh1, of the fission **yeast** Schizosaccharomyces pombe encoding a GTP-binding protein of 201 amino acids and belonging to the ras superfamily was isolated using the protein-coding region of the cloned Saccharomyces cerevisiae YPT1 gene as hybridization probe. The ryh1 gene is interrupted by three introns. ryh1 null mutants are viable but unable to grow at temperatures greater than **35**.5 degrees C. Invertase of ryh1- cells is properly secreted but has a faster electrophoretic mobility compared to that of wild-type cells. The **temperature-sensitive** phenotype of ryh1 null mutants is complemented by the human rab6 cDNA expressed either under transcriptional control of the S.pombe adh or the SV40 early **promoter**.

L7 ANSWER 23 OF 26 MEDLINE
AN 90275617 MEDLINE
DN 90275617
TI NSP1: a **yeast** nuclear envelope protein localized at the nuclear pores exerts its essential function by its carboxy-terminal domain.
AU Nehrbass U; Kern H; Mutvei A; Horstmann H; Marshallsay B; Hurt E C
CS European Molecular Biology Laboratory, Heidelberg, Federal Republic of Germany..
SO CELL, (1990 Jun 15) 61 (6) 979-89.
Journal code: CQ4. ISSN: 0092-8674.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199009
AB NSP1 is located at the nuclear periphery in **yeast** and is essential for cell growth. Employing immunoelectron microscopy on **yeast** cells, we show that NSP1 is located at the nuclear pores. The molecular analysis of the NSP1 protein points to a two domain model: a nonessential domain (the first 603 amino acids) composed of repetitive sequences common to other nuclear proteins and an essential, carboxy-terminal domain (residues 604-823) mediating the vital function of NSP1. The NSP1 carboxy-terminal domain, which shows a heptad repeat organization, affected the correct location of two nuclear proteins: site-specific amino acid substitutions within a predicted alpha-helical structure of this domain caused a **temperature-sensitive** growth arrest at **37** degrees C and the appearance of NSP1 and NOP1, a nucleolar protein, in the cytosol.

L7 ANSWER 24 OF 26 MEDLINE DUPLICATE 13
AN 90128227 MEDLINE
DN 90128227
TI Isolation and characterization of **temperature-sensitive** mutations in the RAS2 and CYR1 genes of Saccharomyces cerevisiae.

galactose-inducible GAL1 **promoter**. A ras1 strain transformed with this plasmid was subjected to ethyl methanesulfonate mutagenesis and nystatin enrichment. Screening of approximately 13,000 mutagenized colonies for galactose-dependent growth at a high **temperature** (**37** degrees) yielded six **temperature-sensitive** ras2 (ras2ts) mutations and one **temperature-sensitive** cyr1 (cyr1ts) mutation that can be suppressed by overexpression or increased dosage of RAS2. Some ras2ts mutations were shown to be suppressed by an extra copy of CYR1. Therefore increased dosage of either RAS2 or CYR1 can suppress the **temperature** sensitivity caused by a mutation in the other. ras1 ras2ts and ras1 cyr1ts mutants arrested in the G1 phase of the cell cycle at the restrictive **temperature**, and showed pleiotropic phenotypes to varying degrees even at a **temperature** permissive for growth (25 degrees), including slow growth, sporulation on rich media, increased accumulation of glycogen, impaired growth on nonfermentable carbon sources, heat-shock resistance, impaired growth on low concentrations of glucose, and lithium sensitivity.

Of these, impaired growth on low concentrations of glucose and sensitivity to lithium are new phenotypes, which have not been reported for mutants defective in the cAMP pathway.

L7 ANSWER 25 OF 26 MEDLINE DUPLICATE 14
AN 84119488 MEDLINE
DN 84119488
TI Regulated expression of a human interferon gene in **yeast**: control by phosphate concentration or **temperature**.
AU Kramer R A; DeChiara T M; Schaber M D; Hilliker S
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1984 Jan) 81 (2) 367-70.
Journal code: PV3. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 198405
AB The **promoter**/regulator region from the **yeast** repressible acid phosphatase gene was used to construct a vector for the regulated expression of cloned genes in **yeast**. The gene for human leukocyte interferon was inserted into this vector. **Yeast** cells transformed with the resulting plasmid produced significant amounts of interferon only when grown in medium lacking inorganic phosphate. Mutants in two acid phosphatase regulatory genes (coding for a defective repressor and a **temperature-sensitive** positive regulator) were used to develop a **yeast** strain that grew well at a high **temperature** (**35** degrees C) but produced interferon only at a low **temperature** (23 degrees C), independent of phosphate concentration.

L7 ANSWER 26 OF 26 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1976:209725 BIOSIS
DN BA62:39725
TI CONTROL OF RNA SYNTHESIS IN EUKARYOTES PART 3 THE EFFECT OF CYCLO HEXIMIDE AND EDEINE ON RNA SYNTHESIS IN **YEAST**.
AU GROSS K J; POGO A O
SO BIOCHEMISTRY, (1976) 15 (10), 2082-2086.
CODEN: BICHAW. ISSN: 0006-2960.
FS BA; OLD
LA Unavailable
AB The addition of cycloheximide to a thermosensitive conditional **yeast** [saccharomyces cerevisiae] mutant (ts-187) before and after transfer to the nonpermissive **temperature** (**36**.degree. C) for initiation of protein synthesis produced the uncoupling of RNA and protein synthetic machineries. Since the drug can produce this relaxation in the presence and absence of protein synthesis, it was concluded that the coupling of protein and RNA synthesis, which a **temperature** shift produced was not exclusively related to the inhibition of protein synthesis. Support for this assumption was obtained using the parental (A364A) strain. Transferring this strain to **36**.degree. C produced inhibition of RNA synthesis in the presence of protein synthesis stimulation. Cycloheximide and edeine prevented the inhibition that

the **promoter**-like factor(s) was a polypeptide different from the RNA polymerase and t least in **yeast**, had a high t ɔver.

L28 ANSWER 1 OF 67 MEDLINE
AN 2000094753 MEDLINE
DN 20094753
TI Synthetic genetic interactions with **temperature-sensitive** clathrin in Saccharomyces cerevisiae. Roles for synaptojanin-like Inp53p and dynamin-related Vps1p in clathrin-dependent protein sorting at the trans-Golgi network.
AU Bensen E S; Costaguta G; Payne G S
CS Department of Biological Chemistry, School of Medicine, University of California, Los Angeles, California 90095, USA.
NC T32-GM07104 (NIGMS)
GM-39040 (NIGMS)
SO GENETICS, (2000 Jan) 154 (1) 83-97.
Journal code: FNH. ISSN: 0016-6731.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200004
EW 20000403
AB Clathrin is involved in selective protein transport at the Golgi apparatus and the plasma membrane. To further understand the molecular mechanisms underlying clathrin-mediated protein transport pathways, we initiated a genetic **screen** for mutations that display synthetic growth defects when combined with a **temperature-sensitive** allele of the clathrin heavy chain gene (chc1-521) in Saccharomyces cerevisiae. Mutations, when present in cells with wild-type clathrin, were analyzed for effects on mating pheromone alpha-factor precursor maturation and sorting of the vacuolar protein carboxypeptidase Y as measures of protein sorting at the **yeast** trans-Golgi network (TGN) compartment. By these criteria, two classes of mutants were obtained, those with and those without defects in protein sorting at the TGN. One **mutant** with unaltered protein sorting at the TGN contains a mutation in PTC1, a type 2c serine/threonine phosphatase with widespread influences. The collection of mutants displaying TGN sorting defects includes members with mutations in previously identified vacuolar protein sorting genes (VPS), including the dynamin family member VPS1. Striking genetic interactions were observed by combining **temperature-sensitive** alleles of CHC1 and VPS1, supporting the model that Vps1p is involved in clathrin-mediated vesicle formation at the TGN. Also in the spectrum of mutants with TGN sorting defects are isolates with mutations in the following: RIC1, encoding a product originally proposed to participate in ribosome biogenesis; LUV1, encoding a product potentially involved in vacuole and microtubule organization; and INP53, encoding a synaptojanin-like inositol polyphosphate 5-phosphatase. Disruption of INP53, but not the related INP51 and INP52 genes, resulted in alpha-factor maturation defects and exacerbated alpha-factor maturation defects when combined with chc1-521. Our findings implicate a wide variety of proteins in clathrin-dependent processes and provide evidence for the selective involvement of Inp53p in clathrin-mediated protein sorting at the TGN.

L28 ANSWER 2 OF 67 MEDLINE
AN 2000069787 MEDLINE
DN 20069787
TI Role for Drs2p, a P-type ATPase and potential aminophospholipid translocase, in **yeast** late Golgi function.
AU Chen C Y; Ingram M F; Rosal P H; Graham T R
CS Department of Molecular Biology, Vanderbilt University, Nashville, Tennessee 37235, USA.
SO JOURNAL OF CELL BIOLOGY, (1999 Dec 13) 147 (6) 1223-36.
Journal code: HMV. ISSN: 0021-9525.

other SEC genes tested. Consistent with these genetic analyses, we found that the drs2Delta **mutant** exhibits late Golgi defects that may result from a loss of clathrin function at this compartment. These include a defect in the Kex2-dependent processing of pro-alpha-factor and the accumulation of abnormal Golgi cisternae. Moreover, we observed a marked reduction in clathrin-coated vesicles that can be isolated from the drs2Delta cells. Subcellular fractionation and immunofluorescence analysis indicate that Drs2p localizes to late Golgi membranes containing Kex2p. These observations indicate a novel role for a P-type ATPase in late Golgi function and suggest a possible link between membrane asymmetry and clathrin function at the Golgi complex.

L28 ANSWER 3 OF 67 MEDLINE
AN 2000029762 MEDLINE
DN 20029762
TI Sec34p, a protein required for vesicle tethering to the **yeast** Golgi apparatus, is in a complex with Sec35p.
AU VanRheenen S M; Cao X; Sapperstein S K; Chiang E C; Lupashin V V; Barlowe C; Waters M G
CS Department of Molecular Biology, Princeton University, Princeton, New Jersey 08544, USA.
NC GM52549 (NIGMS)
GM07312 (NIGMS)
SO JOURNAL OF CELL BIOLOGY, (1999 Nov 15) 147 (4) 729-42.
Journal code: HMV. ISSN: 0021-9525.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 200002
EW 20000204
AB A **screen** for mutants of Saccharomyces cerevisiae secretory pathway components previously yielded sec34, a **mutant** that accumulates numerous vesicles and fails to transport proteins from the ER to the Golgi complex at the restrictive **temperature** (Wuestehube, L.J., R. Duden, A. Eun, S. Hamamoto, P. Korn, R. Ram, and R. Schekman. 1996. Genetics. 142:393-406). We find that SEC34 encodes a novel protein of 93-kD, peripherally associated with membranes. The **temperature -sensitive** phenotype of sec34-2 is suppressed by the rab GTPase Ypt1p that functions early in the secretory pathway, or by the dominant form of the ER to Golgi complex target-SNARE (soluble N-ethylmaleimide **sensitive** fusion protein attachment protein receptor)-associated protein Sly1p, Sly1-20p. Weaker suppression is evident upon overexpression of genes encoding the vesicle tethering factor Uso1p or the vesicle-SNAREs Sec22p, Bet1p, or Ykt6p. This genetic suppression profile is similar to that of sec35-1, a **mutant** allele of a gene encoding an ER to Golgi vesicle tethering factor and, like Sec35p, Sec34p is required in vitro for vesicle tethering. sec34-2 and sec35-1 display a synthetic lethal interaction, a genetic result explained by the finding that Sec34p and Sec35p can interact by two-hybrid analysis. Fractionation of **yeast** cytosol indicates that Sec34p and Sec35p exist in an approximately 750-kD protein complex. Finally, we describe RUD3, a novel gene identified through a genetic **screen** for multicopy suppressors of a mutation in USO1, which suppresses the sec34-2 mutation as well.

L28 ANSWER 4 OF 67 MEDLINE
AN 1999443788 MEDLINE
DN 99443788
TI High-copy suppressor analysis reveals a physical interaction between Sec34p and Sec35p, a protein implicated in vesicle docking.
AU Kim D W; Sacher M; Scarpa A; Quinn A M; Ferro-Novick S
CS Howard Hughes Medical Institute and the Department of Cell Biology, Yale University School of Medicine, New Haven, Connecticut 06510, USA.
SO MOLECULAR BIOLOGY OF THE CELL, (1999 Oct) 10 (10) 3317-29.
Journal code: BAU. ISSN: 1059-1524.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)

ER-to-Golgi transport, but not with those that block the budding of vesicles from the [redacted]. Our findings suggest that Grp[redacted] may facilitate membrane traffic indirectly, possibly by maintaining Golgi function. In an effort to identify genes whose products physically interact with Sec34p, we also tested the ability of overexpressed SEC34 to suppress known secretory mutations that block vesicular traffic between the ER and the Golgi. This **screen** revealed that SEC34 specifically suppresses sec35-1. SEC34 encodes a hydrophilic protein of approximately 100 kDa. Like Sec35p, which has been implicated in the tethering of ER-derived vesicles to the Golgi, Sec34p is predominantly soluble. Sec34p and Sec35p stably associate with each other to form a multiprotein complex of approximately 480 kDa. These data indicate that Sec34p acts in conjunction with Sec35p to mediate a common step in vesicular traffic.

L28 ANSWER 5 OF 67 MEDLINE
AN 1999432251 MEDLINE
DN 99432251
TI CDC45 and DPB11 are required for processive DNA replication and resistance to DNA topoisomerase I-mediated DNA damage.
AU Reid R J; Fiorani P; Sugawara M; Bjornsti M A
CS Department of Biochemistry, Thomas Jefferson University, Philadelphia, PA 19107, USA.
NC CA58755 (NCI)
CA70406 (NCI)
CA21675 (NCI)
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1999 Sep 28) 96 (20) 11440-5.
Journal code: PV3. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199912
EW 19991204
AB The antitumor agent camptothecin targets DNA topoisomerase I by reversibly stabilizing a covalent enzyme-DNA intermediate. The subsequent collision of DNA replication forks with these drug-enzyme-DNA complexes produces the cytotoxic DNA lesions that signal cell cycle arrest and ultimately lead to cell death. Despite intense investigation, the character of the lesions produced and the repair processes that resolve the damage remain poorly defined. A **yeast** genetic **screen** was implemented to isolate conditional mutants with enhanced sensitivity to DNA topoisomerase I-mediated DNA damage. Cells exhibiting **temperature-sensitive** growth in the presence of the DNA topoisomerase I **mutant**, Top1T722Ap, were selected. Substitution of Ala for Thr722 increases the stability of the covalent Top1T722Ap-DNA intermediate, mimicking the cytotoxic action of camptothecin. Two mutants isolated, cdc45-10 and dpb11-10, exhibited specific defects in DNA replication and a synthetic lethal phenotype in the absence of DNA damaging agents. The accumulation of Okazaki fragments under nonpermissive conditions suggests a common function in promoting processive DNA replication through polymerase switching. These results provide a mechanistic basis for understanding the cellular processes involved in the resolution of DNA damage induced by camptothecin and DNA topoisomerase I.

L28 ANSWER 6 OF 67 MEDLINE
AN 1999419035 MEDLINE
DN 99419035
TI The Saccharomyces cerevisiae HCR1 gene encoding a homologue of the p35 subunit of human translation initiation factor 3 (eIF3) is a high copy suppressor of a **temperature-sensitive** mutation in the Rpg1p subunit of **yeast** eIF3.
AU Valasek L; Hasek J; Trachsel H; Imre E M; Ruis H
CS Vienna Biocenter, Institute of Biochemistry and Molecular Cell Biology, University of Vienna, A-1030 Vienna, Austria..

binding to 40 S ribosomal subunits. Recently, we described the identification of RPG1 (TIF32), the p110 subunit of the eIF3 core complex in **yeast**. In a **screen** for Saccharomyces cerevisiae multicopy suppressors of the rpg1-1 **temperature-sensitive mutant**, an unknown gene corresponding to the open reading frame YLR192C was identified. When overexpressed, the 30-kDa gene product, named Hcr1p, was able to support, under restrictive conditions, growth of the rpg1-1 **temperature-sensitive mutant**, but not of a Rpg1p-depleted **mutant**. An hcr1 null **mutant** was viable, but showed slight reduction of growth when compared with the wild-type strain. Physical interaction between the Hcr1 and Rpg1 proteins was shown by co-immunoprecipitation analysis. The combination of Deltahcr1 and rpg1-1 mutations resulted in a synthetic enhancement of the slow growth phenotype at a semipermissive **temperature**. In a computer search, a significant homology to the human p35 subunit of the eIF3 complex was found. We assume that the **yeast** Hcr1 protein participates in translation initiation likely as a protein associated with the eIF3 complex.

L28 ANSWER 7 OF 67 MEDLINE
AN 1999402992 MEDLINE
DN 99402992
TI **Temperature-sensitive** mutations in the Saccharomyces cerevisiae MRT4, GRC5, SLA2 and THS1 genes result in defects in mRNA turnover.
AU Zuk D; Belk J P; Jacobson A
CS Department of Molecular Genetics and Microbiology, University of Massachusetts Medical School, Worcester, Massachusetts 01655, USA.
NC GM-27757 (NIGMS)
T32-HD07312-14 (NICHD)
SO GENETICS, (1999 Sep) 153 (1) 35-47.
Journal code: FNH. ISSN: 0016-6731.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200001
EW 20000104
AB In a **screen** for factors involved in mRNA turnover, four **temperature-sensitive yeast** strains (ts1189, ts942, ts817, and ts1100) exhibited defects in the decay of several mRNAs.
Complementation of the growth and mRNA decay defects, and genetic experiments, revealed that ts1189 is mutated in the previously unknown MRT4 gene, ts942 is mutated in GRC5 (encoding the L9 ribosomal protein), ts817 contains a mutation in SLA2 (encoding a membrane protein), and ts1100 contains a mutation in THS1 (encoding the threonyl-tRNA synthetase). Three of the four mutants (mrt4, grc5, and sla2) were not defective in protein synthesis, suggesting that these strains contain mutations in factors that may play a specific role in mRNA decay. The mRNA stabilization observed in the ths1 strain, however, could be due to the significant drop in translation observed in this **mutant** at 37 degrees. While the three interesting mutants appear to encode novel mRNA decay factors, at least one could be linked to a previously characterized mRNA decay pathway. The growth and mRNA decay defects of ts942 (grc5) cells were suppressed by overexpression of the NMD3 gene, encoding a protein shown to participate in a two-hybrid interaction with the nonsense-mediated decay protein Upf1p.

L28 ANSWER 8 OF 67 MEDLINE
AN 1999320819 MEDLINE
DN 99320819
TI A mutation in the secretion pathway of the **yeast** Yarrowia lipolytica that displays synthetic lethality in combination with a mutation affecting the signal recognition particle.
AU Boisrame A; Beckerich J M; Gaillardin C
CS Laboratoire de Genetique moleculaire et cellulaire INRA, CNRS, Institut National Agronomique Paris-Grignon, Thiverval-Grignon, France.. boisrame@cardere.grignon.inra.fr
SO MOLECULAR AND GENERAL GENETICS, (1999 Jun) 261 (4-5) 601-9.
Journal code: NGP. ISSN: 0026-8925.
CY GERMANY: Germany, Federal Republic of

sls2-1, was isolated that causes synthetic lethality when combined with the 7S RNA mutation. On its own, the sls2-1 mutation confers a **temperature-sensitive** growth phenotype. The secretory phenotype of the sls2 **mutant** consists in abnormal secretion of several polypeptides, and thus differs from the defect in secretory protein synthesis associated with the 7S RNA and sls1-1 mutations. Two new Y. lipolytica genes were identified which can relieve the growth defect of sls2-1 cells: SLS2 itself and SSL2, a multicopy suppressor of the **temperature** sensitivity of the sls2 **mutant**. The SLS2 gene encodes a polypeptide that can potentially be farnesylated and phosphorylated, and shares some homology with an S. cerevisiae protein of unknown function. Ssl2p resembles calmodulin-dependent serine/threonine protein kinases. These two proteins may interact to regulate protein sorting.

L28 ANSWER 9 OF 67 MEDLINE
AN 1999262966 MEDLINE
DN 99262966
TI A TATA-binding protein **mutant** defective for TFIID complex formation in vivo.
AU Ranallo R T; Struhl K; Stargell L A
CS Biochemistry and Molecular Biology, Colorado State University, Fort Collins, Colorado 80523-1870, USA.
NC GM30186 (NIGMS)
GM56884 (NIGMS)
SO MOLECULAR AND CELLULAR BIOLOGY, (1999 Jun) 19 (6) 3951-7.
Journal code: NGY. ISSN: 0270-7306.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199908
EW 19990803
AB Using an intragenic complementation **screen**, we have identified a **temperature-sensitive** TATA-binding protein (TBP) **mutant** (K151L, K156Y) that is defective for interaction with certain **yeast** TBP-associated factors (TAFs) at the restrictive **temperature**. The K151L,K156Y **mutant** appears to be functional for RNA polymerase I (Pol I) and Pol III transcription, and it is capable of supporting Gal4-activated and Gcn4-activated transcription by Pol II. However, transcription from certain TATA-containing and TATA-less Pol II promoters is reduced at the restrictive **temperature**. Immunoprecipitation analysis of extracts prepared after culturing cells at the restrictive **temperature** for 1 h indicates that the K151L,K156Y derivative is severely compromised in its ability to interact with TAF130, TAF90, TAF68/61, and TAF25 while remaining functional for interaction with TAF60 and TAF30. Thus, a TBP **mutant** that is compromised in its ability to form TFIID can support the response to Gcn4 but is defective for transcription from specific promoters in vivo.

L28 ANSWER 10 OF 67 MEDLINE
AN 1999157005 MEDLINE
DN 99157005
TI Caffeine can override the S-M checkpoint in fission **yeast**.
AU Wang S W; Norbury C; Harris A L; Toda T
CS Imperial Cancer Research Fund, Cell Regulation Laboratory, PO Box 123, Lincoln's Inn Fields, London WC2 A3P, UK.
SO JOURNAL OF CELL SCIENCE, (1999 Mar) 112 (Pt 6) 927-37.
Journal code: HNK. ISSN: 0021-9533.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199907
EW 19990702
AB The replication checkpoint (or 'S-M checkpoint') control prevents progression into mitosis when DNA replication is incomplete. Caffeine has been known for some time to have the capacity to override the S-M checkpoint in animal cells. We show here that caffeine also disrupts the S-M checkpoint in the fission **yeast** Schizosaccharomyces pombe.

S phase arrest. In addition, the same combination of drugs was specifically tolerated in cells overexpressing either of two novel S. pombe genes isolated in a cDNA library **screen**. These findings should allow further molecular investigation of the regulation of S phase arrest, and may provide a useful system with which to identify novel drugs that specifically abrogate the checkpoint control.

L28 ANSWER 11 OF 67 MEDLINE
AN 1999084996 MEDLINE
DN 99084996
TI Mutations in a peptidylprolyl-cis/trans-isomerase gene lead to a defect in 3'-end formation of a pre-mRNA in Saccharomyces cerevisiae.
AU Hani J; Schelbert B; Bernhardt A; Domdey H; Fischer G; Wiebauer K; Rahfeld J U
CS Genzentrum der Ludwig-Maximilians-Universitat Munchen, Feodor-Lynen Strasse 25, 81377 Munchen, Germany.
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1999 Jan 1) 274 (1) 108-16.
Journal code: HIV. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Cancer Journals; Priority Journals
EM 199904
AB In a genetic **screen** aimed at the identification of trans-acting factors involved in mRNA 3'-end processing of budding **yeast**, we have previously isolated two **temperature-sensitive** mutants with an apparent defect in the 3'-end formation of a plasmid-derived pre-mRNA. Surprisingly, both mutants were rescued by the essential gene ESS1/PTF1 that encoded a putative peptidylprolyl-cis/trans-isomerase (PPIase) (Hani, J., Stumpf, G., and Domdey, H. (1995) FEBS Lett. 365, 198-202). Such enzymes, which catalyze the cis/trans-interconversion of peptide bonds N-terminal of prolines, are suggested to play a role in protein folding or trafficking. Here we report that Ptf1p shows PPIase activity in vitro, displaying an unusual substrate specificity for peptides with phosphorylated serine and threonine residues preceding proline. Both mutations were found to result in amino acid substitutions of highly conserved residues within the PPIase domain, causing a marked decrease in PPIase activity of the **mutant** enzymes. Our results are suggestive of a so far unknown involvement of a PPIase in mRNA 3'-end formation in Saccharomyces cerevisiae.

L28 ANSWER 12 OF 67 MEDLINE
AN 1999077995 MEDLINE
DN 99077995
TI Elevated levels of a U4/U6.U5 snRNP-associated protein, Spp381p, rescue a **mutant** defective in spliceosome maturation.
AU Lybarger S; Beickman K; Brown V; Dembla-Rajpal N; Morey K; Seipelt R; Rymond B C
CS T. H. Morgan School of Biological Sciences and The Markey Cancer Center, University of Kentucky, Lexington, Kentucky 40506-0225, USA.
NC GM42476 (NIGMS)
SO MOLECULAR AND CELLULAR BIOLOGY, (1999 Jan) 19 (1) 577-84.
Journal code: NGY. ISSN: 0270-7306.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199904
EW 19990402
AB U4 snRNA release from the spliceosome occurs through an essential but ill-defined Prp38p-dependent step. Here we report the results of a dosage suppressor **screen** to identify genes that contribute to PRP38 function. Elevated expression of a previously uncharacterized gene, SPP381, efficiently suppresses the growth and splicing defects of a **temperature-sensitive** (Ts) **mutant** prp38-1.
This suppression is specific in that enhanced SPP381 expression does not alter the abundance of intronless RNA transcripts or suppress the Ts phenotypes of other prp mutants. Since SPP381 does not suppress a

acidic proteins without obvious RNA binding domains, Spp381p and Prp38p, act in concert to mote U4/U5.U6 tri-snRNP functi[redacted] in the spliceosome cycle.

L28 ANSWER 13 OF 67 MEDLINE
AN 1999063405 MEDLINE
DN 99063405
TI Two **mutant** forms of the S1/TPR-containing protein Rrp5p affect the 18S rRNA synthesis in Saccharomyces cerevisiae.
AU Torchet C; Jacq C; Hermann-Le Denmat S
CS Laboratoire de Genetique Moleculaire, Ecole Normale Superieure, URA C.N.R.S. 1302, Paris, France.
SO RNA, (1998 Dec) 4 (12) 1636-52.
Journal code: CHB. ISSN: 1355-8382.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199903
EW 19990301
AB The genetic depletion of **yeast** Rrp5p results in a synthesis defect of both 18S and 5.8S ribosomal RNAs (Venema J, Tollervey D. 1996. EMBO J 15:5701-5714). We have isolated the RRP5gene in a genetic approach aimed to select for **yeast** factors interfering with protein import into mitochondria. We describe here a striking feature of Rrp5p amino acid sequence, namely the presence of twelve putative S1 RNA-binding motifs and seven tetratricopeptide repeats (TPR) motifs. We have constructed two conditional **temperature-sensitive** alleles of RRP5 gene and analyzed them for associated rRNA-processing defects. First, a functional "bipartite gene" was generated revealing that the S1 and TPR parts of the protein can act independently of each other. We also generated a two amino acid deletion in TPR unit 1 (rrp5delta6 allele). The two **mutant** forms of Rrp5p were shown to cause a defect in 18S rRNA synthesis with no detectable effects on 5.8S rRNA production. However, the rRNA processing pathway was differently affected in each case. Interestingly, the ROK1 gene which, like RRP5, was previously isolated in a **screen** for synthetic lethal mutations with snR10 deletion, was here identified as a high copy suppressor of the rrp5delta6 **temperature-sensitive** allele. ROK1 also acts as a low copy suppressor but cannot bypass the cellular requirement for RRP5. Furthermore, we show that suppression by the Rok1p putative RNA helicase rescues the 18S rRNA synthesis defect caused by the rrp5delta6 mutation.

L28 ANSWER 14 OF 67 MEDLINE
AN 1999029894 MEDLINE
DN 99029894
TI Synthetic lethal interactions with conditional poly(A) polymerase alleles identify LCP5, a gene involved in 18S rRNA maturation.
AU Wiederkehr T; Pretot R F; Minvielle-Sebastia L
CS Department of Cell Biology, Biozentrum, University of Basel, Switzerland.
SO RNA, (1998 Nov) 4 (11) 1357-72.
Journal code: CHB. ISSN: 1355-8382.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199902
EW 19990204
AB To identify new genes involved in 3'-end formation of mRNAs in Saccharomyces cerevisiae, we carried out a **screen** for synthetic lethal mutants with the conditional poly(A) polymerase allele, pap1-7. Five independent **temperature-sensitive** mutations called Icp1 to Icp5 (for lethal with conditional pap1 allele) were isolated. Here, we describe the characterization of the essential gene LCP5 which codes for a protein with a calculated molecular mass of 40.8 kD. Unexpectedly, we found that mutations in LCP5 caused defects in pre-ribosomal RNA (pre-rRNA) processing, whereas mRNA 3'-end formation in vitro was comparable to wild-type. Early cleavage steps (denoted A0 to A2)

reductase is identified in a **screen** for **temperature-sensitive** suppress[redacted] of the Ca2+-**sensitive** csg2Del[redacted] **mutant.**

AU Beeler T; Bacikova D; Gable K; Hopkins L; Johnson C; Slife H; Dunn T
CS Department of Biochemistry, Uniformed Services University of the Health Sciences, Bethesda, Maryland 20814, USA.
NC GM51891 (NIGMS)
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1998 Nov 13) 273 (46) 30688-94. Journal code: HIV. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199902
EW 19990204
AB Saccharomyces cerevisiae csg2Delta mutants accumulate the sphingolipid inositolphosphorylceramide, which renders the cells Ca2+-**sensitive** . **Temperature-sensitive** mutations that suppress the Ca2+ sensitivity of csg2Delta mutants were isolated and characterized to identify genes that encode sphingolipid synthesis enzymes. These **temperature-sensitive** csg2Delta suppressors (tsc) fall into 15 complementation groups. The TSC10/YBR265w gene was found to encode 3-ketosphinganine reductase, the enzyme that catalyzes the second step in the synthesis of phytosphingosine, the long chain base found in **yeast** sphingolipids. 3-Ketosphinganine reductase (Tsc10p) is essential for growth in the absence of exogenous dihydrosphingosine or phytosphingosine. Tsc10p is a member of the short chain dehydrogenase/reductase protein family. The tsc10 mutants accumulate 3-ketosphinganine and microsomal membranes isolated from tsc10 mutants have low 3-ketosphinganine reductase activity. His6-tagged Tsc10p was expressed in Escherichia coli and isolated by nickel-nitrilotriacetic acid column chromatography. The recombinant protein catalyzes the NADPH-dependent reduction of 3-ketosphinganine. These data indicate that Tsc10p is necessary and sufficient for catalyzing the NADPH-dependent reduction of 3-ketosphinganine to dihydrosphingosine.

L28 ANSWER 16 OF 67 MEDLINE
AN 1999016041 MEDLINE
DN 99016041
TI Genetic and morphological analyses reveal a critical interaction between the C-termini of two SNARE proteins and a parallel four helical arrangement for the exocytic SNARE complex.
AU Katz L; Hanson P I; Heuser J E; Brennwald P
CS Department of Cell Biology and Graduate Program in Cell Biology and Genetics, Cornell University Medical College, New York, NY 10021, USA.
NC GM54712 (NIGMS)
GM29647 (NIGMS)
SO EMBO JOURNAL, (1998 Nov 2) 17 (21) 6200-9. Journal code: EMB. ISSN: 0261-4189.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199903
EW 19990303
AB In a **screen** for suppressors of a **temperature-sensitive** mutation in the **yeast** SNAP-25 homolog, Sec9, we have identified a gain-of-function mutation in the **yeast** synaptobrevin homolog, Snc2. The genetic properties of this suppression point to a specific interaction between the C-termini of Sec9 and Snc2 within the SNARE complex. Biochemical analysis of interactions between the wild-type and **mutant** proteins confirms this prediction, demonstrating specific effects of these mutations on interactions between the SNAREs. The location of the mutations suggests that the C-terminal H2 helical domain of Sec9 is likely to be aligned in parallel with Snc2 in the SNARE complex. To test this prediction, we examined the structure of the **yeast** exocytic SNARE complex by deep-etch electron microscopy. Like the neuronal SNARE complex, it is a rod approximately 14 nm long. Using epitope tags, antibodies and maltose-binding protein markers, we find that the helical domains of Sso, Snc and both halves of

vacuolar vital dyes.
AU Zheng B; Wu J N; [redacted]ber W; Lewis D E; Vida T [redacted]
CS Department of Integrative Biology, Pharmacology, and Physiology, University of Texas Medical School, Houston, TX 77030, USA.
NC GM52092 (NIGMS)
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1998 Sep 29) 95 (20) 11721-6.
Journal code: PV3. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199812
EW 19981204
AB An application of flow cytometric sorting is used for isolation of Saccharomyces cerevisiae mutants that mislocalize vacuolar vital dyes. This **screen** is based on the ability of a lipophilic styryl compound, N-(3-triethylammoniumpropyl)-4-(6-(4-(diethylamino)phenyl)hexatrie nyl)pyridinium dibromide (FM4-64), to label endocytic intermediates from the plasma membrane to the vacuole membrane at 15 degreesC. Cells stained at 15 degreesC for both FM4-64 and carboxydichlorofluorescein diacetate (a vacuolar luminal vital stain), had a pronounced shift in red/green fluorescence from cells stained at 30 degrees or 38 degreesC. Flow cytometric selection based on this characteristic shift allowed the isolation of 16 mutants. These comprised 12 complementation groups, which we have designated SVL for styryl dye vacuolar localization. These groups were put into three classes. Class I mutants contain very large vacuoles; class II mutants have very fragmented vacuoles; and class III mutants show the strongest svl phenotype with punctate/diffuse FM4-64 staining. Limited genetic overlap was observed with previously isolated mutants, namely svl2/vps41, svl6/vps16, and svl7/fab1. The remaining svl mutants appear to represent novel genes, two of which showed **temperature-sensitive** vacuole staining morphology. Another **mutant**, svl8, displayed defects in uptake and sorting of phosphatidylcholine and phosphatidylethanolamine. Our flow cytometric strategy may be useful for isolation of other mutants where mislocalization of fluorescent compounds can be detected.

L28 ANSWER 18 OF 67 MEDLINE
AN 1998418669 MEDLINE
DN 98418669
TI The SH2-containing adapter protein GRB10 interacts with BCR-ABL.
AU Bai R Y; Jahn T; Schrem S; Munzert G; Weidner K M; Wang J Y; Duyster J
CS Department of Internal Medicine III, Technical University of Munich, Germany.
SO ONCOGENE, (1998 Aug 27) 17 (8) 941-8.
Journal code: ONC. ISSN: 0950-9232.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199812
AB Bcr-Abl is an oncogenic tyrosine kinase expressed in tumor cells of CML and a subset of ALL which in its unregulated and activated state is thought to cause cell transformation and leukemia. Bcr-Abl contains several autophosphorylation sites which serve as potential docking sites for SH2-containing signaling molecules. Mutational analysis has indicated that these autophosphorylation sites play a critical role in the transforming capability of Bcr-Abl. It has been shown that the SH2-containing adapter protein Grb2 binds to the autophosphorylation site Tyr(p)177 whereby it couples Bcr-Abl to the Ras pathway. The biological consequences of this interaction, however, are presently unclear. A Tyr177-mutated Bcr-Abl which lacks the ability to interact with the Grb2-SH2 domain still transforms myeloid cells and generates tumors in nude mice. We performed a **yeast** two-hybrid **screen** to identify signaling proteins which bind to distinct Bcr-Abl autophosphorylation sites. Autophosphorylation of Bcr-Abl in **yeast** was accomplished by using the DNA binding protein LexA which permits dimerization and crossphosphorylation of the fused bait. Using a LexA-Bcr-Abl full length fusion protein as bait, we identified several

as shown by co-immunoprecipitation analysis in CML cells. Using a **temperature sensitive** Bcr-Abl stably overexpressed hematopoetic cells, we demonstrated that complex formation of Grb10 with Bcr-Abl was kinase activation-dependent in vivo. Notably, a Bcr-Abl **mutant** protein (Bcr/1-242-Abl) which lacks the ability to interact with Grb10 partially alleviated IL-3 dependence of Ba/F3 cells, indicating that the Grb10/Bcr-Abl interaction is important for Bcr-Abl-induced IL-3 independence of Ba/F3 cells. In addition, the Bcr/1-242-Abl **mutant** has a reduced capacity to induce focus formation in fibroblasts.

L28 ANSWER 19 OF 67 MEDLINE
AN 1998378563 MEDLINE
DN 98378563
TI A novel function of the DNA repair gene rhp6 in mating-type silencing by chromatin remodeling in fission **yeast**.
AU Singh J; Goel V; Klar A J
CS Institute of Microbial Technology, Sector 39 A, Chandigarh 160 036, Punjab, India.. Jag@koel.imtech.ernet.in
SO MOLECULAR AND CELLULAR BIOLOGY, (1998 Sep) 18 (9) 5511-22.
Journal code: NGY. ISSN: 0270-7306.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199811
EW 19981102
AB Recent studies have indicated that the DNA replication machinery is coupled to silencing of mating-type loci in the budding **yeast** Saccharomyces cerevisiae, and a similar silencing mechanism may operate in the distantly related **yeast** Schizosaccharomyces pombe. Regarding gene regulation, an important function of DNA replication may be in coupling of faithful chromatin assembly to reestablishment of the parental states of gene expression in daughter cells. We have been interested in isolating mutants that are defective in this hypothesized coupling. An S. pombe **mutant** fortuitously isolated from a **screen** for **temperature-sensitive** growth and silencing phenotype exhibited a novel defect in silencing that was dependent on the switching competence of the mating-type loci, a property that differentiates this **mutant** from other silencing mutants of S. pombe as well as of S. cerevisiae. This unique **mutant** phenotype defined a locus which we named sng1 (for silencing not governed). Chromatin analysis revealed a switching-dependent unfolding of the donor loci mat2P and mat3M in the sng1(-) **mutant**, as indicated by increased accessibility to the in vivo-expressed Escherichia coli dam methylase. Unexpectedly, cloning and sequencing identified the gene as the previously isolated DNA repair gene rhp6. RAD6, an rhp6 homolog in S. cerevisiae, is required for postreplication DNA repair and ubiquitination of histones H2A and H2B. This study implicates the Rad6/rhp6 protein in gene regulation and, more importantly, suggests that a transient window of opportunity exists to ensure the remodeling of chromatin structure during chromosome replication and recombination. We propose that the effects of the sng1(-)/rhp6(-) mutation on silencing are indirect consequences of changes in chromatin structure.

L28 ANSWER 20 OF 67 MEDLINE
AN 1998378543 MEDLINE
DN 98378543
TI Vam7p, a SNAP-25-like molecule, and Vam3p, a syntaxin homolog, function together in **yeast** vacuolar protein trafficking.
AU Sato T K; Darsow T; Emr S D
CS Division of Cellular and Molecular Medicine and Department of Biology, Howard Hughes Medical Institute, University of California at San Diego School of Medicine, La Jolla, California 92093-0668, USA.
NC CA58689 (NCI)
SO MOLECULAR AND CELLULAR BIOLOGY, (1998 Sep) 18 (9) 5308-19.
Journal code: NGY. ISSN: 0270-7306.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English

the nonpermissive **temperature** displayed rapid defects in the delivery of multip[redacted] proteins that traffic to the v[redacted]uole via distinct biosynthetic pathw[redacted]s. Examination of vam7(tsf) cel[redacted] at the nonpermissive **temperature** by electron microscopy revealed the accumulation of aberrant membranous compartments that may represent unfused transport intermediates. A fraction of Vam7p was localized to vacuolar membranes. Furthermore, VAM7 displayed genetic interactions with the vacuolar syntaxin homolog, VAM3. Consistent with the genetic results, Vam7p physically associated in a complex containing Vam3p, and this interaction was enhanced by inactivation of the **yeast** NSF (N-ethyl maleimide-**sensitive** factor) homolog, Sec18p. In addition to the coiled-coil domain, Vam7p also contains a putative NADPH oxidase p40(phox) (PX) domain. Changes in two conserved amino acids within this domain resulted in synthetic phenotypes when combined with the vam3(tsf) mutation, suggesting that the PX domain is required for Vam7p function. This study provides evidence for the functional and physical interaction between Vam7p and Vam3p at the vacuolar membrane, where they function as part of a t-SNARE complex required for the docking and/or fusion of multiple transport intermediates destined for the vacuole.

L28 ANSWER 21 OF 67 MEDLINE
AN 1998359841 MEDLINE
DN 98359841
TI A genetic analysis of interactions with Spc110p reveals distinct functions of Spc97p and Spc98p, components of the **yeast** gamma-tubulin complex.
AU Nguyen T; Vinh D B N; Crawford D K; Davis T N
CS Molecular and Cellular Biology Program, University of Washington, Seattle, Washington 98195, USA.
NC GM-40506 (NIGMS)
T32 GM-07270 (NIGMS)
F32 GM-17946 (NIGMS)
SO MOLECULAR BIOLOGY OF THE CELL, (1998 Aug) 9 (8) 2201-16.
Journal code: BAU. ISSN: 1059-1524.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199812
EW 19981201
AB The spindle pole body (SPB) in Saccharomyces cerevisiae functions as the microtubule-organizing center. Spc110p is an essential structural component of the SPB and spans between the central and inner plaques of this multilamellar organelle. The amino terminus of Spc110p faces the inner plaque, the substructure from which spindle microtubules radiate. We have undertaken a synthetic lethal **screen** to identify mutations that enhance the phenotype of the **temperature-sensitive** spc110-221 allele, which encodes mutations in the amino terminus. The **screen** identified mutations in SPC97 and SPC98, two genes encoding components of the Tub4p complex in **yeast**. The spc98-63 allele is synthetic lethal only with spc110 alleles that encode mutations in the N terminus of Spc110p. In contrast, the spc97 alleles are synthetic lethal with spc110 alleles that encode mutations in either the N terminus or the C terminus. Using the two-hybrid assay, we show that the interactions of Spc110p with Spc97p and Spc98p are not equivalent. The N terminus of Spc110p displays a robust interaction with Spc98p in two different two-hybrid assays, while the interaction between Spc97p and Spc110p is not detectable in one strain and gives a weak signal in the other. Extra copies of SPC98 enhance the interaction between Spc97p and Spc110p, while extra copies of SPC97 interfere with the interaction between Spc98p and Spc110p. By testing the interactions between **mutant** proteins, we show that the lethal phenotype in spc98-63 spc110-221 cells is caused by the failure of Spc98-63p to interact with Spc110-221p. In contrast, the lethal phenotype in spc97-62 spc110-221 cells can be attributed to a decreased interaction between Spc97-62p and Spc98p. Together, these studies provide evidence that Spc110p directly links the Tub4p complex to the SPB. Moreover, an interaction between Spc98p and the amino-terminal

NC GM-07347 (NIGMS)
CA-09370 (NCI)
SO GENETICS, (1998 Jul) 149 (3) 1221-33.
Journal code: FNH. ISSN: 0016-6731.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-AF075169; GENBANK-AF085329
EM 199810
AB A mutation within the Schizosaccharomyces pombe cdc24(+) gene was identified previously in a **screen** for cell division cycle mutants and the cdc24(+) gene was determined to be essential for S phase in this **yeast**. We have isolated the cdc24(+) gene by complementation of a new **temperature-sensitive** allele of the gene, cdc24-G1. The DNA sequence predicts the presence of an open reading frame punctuated by six introns which encodes a pioneer protein of 58 kD. A cdc24 null **mutant** was generated by homologous recombination. Haploid cells lacking cdc24(+) are inviable, indicating that cdc24(+) is an essential gene. The transcript of cdc24(+) is present at constant levels throughout the cell cycle. Cells lacking cdc24(+) function show a checkpoint-dependent arrest with a 2N DNA content, indicating a block late in S phase. Arrest is accompanied by a rapid loss of viability and chromosome breakage. An S. pombe homolog of the replicative DNA helicase DNA2 of S. cerevisiae suppresses cdc24. These results suggest that Cdc24p plays a role in the progression of normal DNA replication and is required to maintain genomic integrity.

L28 ANSWER 23 OF 67 MEDLINE
AN 1998278802 MEDLINE
DN 98278802
TI A high copy suppressor **screen** reveals genetic interactions between BET3 and a new gene. Evidence for a novel complex in ER-to-Golgi transport.
AU Jiang Y; Scarpa A; Zhang L; Stone S; Feliciano E; Ferro-Novick S
CS Howard Hughes Medical Institute, Yale University School of Medicine, New Haven, Connecticut 06510, USA.
SO GENETICS, (1998 Jun) 149 (2) 833-41.
Journal code: FNH. ISSN: 0016-6731.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-AA203173
EM 199811
EW 19981102
AB The BET3 gene in the **yeast** Saccharomyces cerevisiae encodes a 22-kD hydrophilic protein that is required for vesicular transport between the ER and Golgi complex. To gain insight into the role of Bet3p, we screened for genes that suppress the growth defect of the **temperature-sensitive** bet3 **mutant** at 34 degrees. This high copy suppressor **screen** resulted in the isolation of a new gene, called BET5. BET5 encodes an essential 18-kD hydrophilic protein that in high copy allows growth of the bet3-1 **mutant**, but not other ER accumulating mutants. This strong and specific suppression is consistent with the fact that Bet3p and Bet5p are members of the same complex. Using PCR mutagenesis, we generated a **temperature-sensitive** mutation in BET5 (bet5-1) that blocks the transport of carboxypeptidase Y to the vacuole and prevents secretion of the **yeast** pheromone alpha-factor at 37 degrees. The precursor forms of these proteins that accumulate in this **mutant** are indicative of a block in membrane traffic between the ER and Golgi apparatus. High copy suppressors of the bet5-1 **mutant** include several genes whose products are required for ER-to-Golgi transport (BET1, SEC22, USO1 and DSS4) and the maintenance of the Golgi (ANP1). These findings support the hypothesis that Bet5p acts in conjunction with Bet3p to mediate a late stage in ER-to-Golgi transport. The identification of mammalian homologues of Bet3p and Bet5p implies that the Bet3p/Bet5p complex is highly conserved in evolution.

EM 199808
EW 19980804
AB Topoisomerase II catalyzes the passage of one DNA helix through another via a transient double-stranded break. The essential nature of this enzyme in cell proliferation and its mechanism of action make it an ideal target for cytotoxic agents. Saccharomyces cerevisiae topoisomerase II has been frequently used as a model for testing potential inhibitors of eukaryotic topoisomerase II as antitumor agents. The standard in vivo method of estimating the sensitivity of S. cerevisiae to the antitopoisomerase drugs is via inhibition or kill curves which rely on viable-cell counts and is labor intensive. We present an alternative to this, a high-throughput in vivo **screen**. This method makes use of a drug-permeable S. cerevisiae strain lacking endogenous topoisomerase II, which is modified to express either human topoisomerase IIalpha or IIbeta or S. cerevisiae topoisomerase II carried on plasmids. Each modified strain expresses a full-length topoisomerase II enzyme, as opposed to the more commonly used **temperature-sensitive** S. cerevisiae **mutant** expressing **yeast** or **yeast**/human hybrid enzymes. A comparison of this new method with a plating-and-counting method gave similar drug sensitivity results, with increased accuracy and reduced manual input for the new method. The information generated has highlighted the sensitivities of different topoisomerase II enzymes and isoenzymes to several different classes of topoisomerase II inhibitor.

L28 ANSWER 25 OF 67 MEDLINE
AN 1998183406 MEDLINE
DN 98183406
TI Cloning and developmental expression of a nuclear ubiquitin-conjugating enzyme (DmUbc9) that interacts with small heat shock proteins in Drosophila melanogaster.
AU Joanisse D R; Inaguma Y; Tanguay R M
CS Laboratoire de Genetique Cellulaire et Developpementale, Pavillon C-E. Marchand, Universite Laval, Sainte-Foy, Quebec, Canada.
SO BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (1998 Mar 6) 244 (1) 102-9.
Journal code: 9Y8. ISSN: 0006-291X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
OS GENBANK-AF030443; GENBANK-AF030444
EM 199806
AB In a two hybrid **screen** designed to identify proteins that interact with small heat shock proteins (sHsps), a Drosophila melanogaster homologue of **yeast** and human ubc9 (Dmubc9) was found to interact with Drosophila Hsp23. Further, two-hybrid system analysis reveals DmUbc9 interaction with Drosophila and mammalian Hsp27. In situ hybridization localizes Dmubc9 as a doublet at locus 21D on chromosome 2L, and genomic cloning of the gene reveals a single open reading frame without introns. The predicted Dmubc9 protein sequence shares a very high level of homology with mouse (85.4%) and human (> or = 82.9%) Ubc9. Genetic complementation analysis show that Dmubc9 functionally rescues a **temperature-sensitive** S. cerevisiae ubc9ts **mutant**. Co-immunoprecipitation with antibody raised against DmUbc9 confirms the interaction with Drosophila Hsp23 and Hsp26 and preferentially with Hsp27. The DmUbc9 protein, which localizes primarily to the nucleus in Drosophila S2 cells, is found at high levels in embryos but is also present at lower levels throughout development. The significance of the sHsp-Ubc9 interaction is discussed.

L28 ANSWER 26 OF 67 MEDLINE
AN 1998130603 MEDLINE
DN 98130603
TI Dob1p (Mtr4p) is a putative ATP-dependent RNA helicase required for the 3' end formation of 5.8S rRNA in Saccharomyces cerevisiae.

essential putative ATP-dependent RNA helicase. Polysome analyses revealed an under accumulation of 60S ribosomal subunits in the dob1-1 **mutant**. Pulse-chase labelling of pre-rRNA showed that this was due to a defect in the synthesis of the 5.8S and 25S rRNAs. Northern and primer extension analyses in the dob1-1 **mutant**, or in a strain genetically depleted of Dob1p, revealed a specific inhibition of the 3' processing of the 5.8S rRNA from its 7S precursor. This processing recently has been attributed to the activity of the exosome, a complex of 3'-->5' exonucleases that includes Rrp4p. In vivo depletion of Dob1p also inhibits degradation of the 5' external transcribed spacer region of the pre-rRNA. A similar phenotype was observed in rrp4 **mutant** strains and, moreover, the dob1-1 and rrp4-1 mutations show a strong synergistic growth inhibition. We propose that Dob1p functions as a cofactor for the exosome complex that unwinds secondary structures in the pre-rRNA that otherwise block the progression of the 3'-->5' exonucleases.

L28 ANSWER 27 OF 67 MEDLINE
AN 1998108017 MEDLINE
DN 98108017
TI Effects of deletion mutations in the **yeast** Ces1 protein on cell growth and morphology and on high copy suppression of mutations in mRNA capping enzyme and translation initiation factor 4A.
AU Schwer B; Linder P; Shuman S
CS Department of Microbiology, Cornell University Medical College, New York, NY 10021, USA.
NC GM52470 (NIGMS)
SO NUCLEIC ACIDS RESEARCH, (1998 Feb 1) 26 (3) 803-9.
Journal code: O8L. ISSN: 0305-1048.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199805
EW 19980502
AB The homologous Saccharomyces cerevisiae genes CES1 and CES4 act as high copy suppressors of **temperature-sensitive** mutations of Ceg1p, the **yeast** mRNA capping enzyme. Neither CES1 nor CES4 is essential for cell growth. We find that a double deletion **mutant** (Delta ces1 Delta ces4) grows at 25-37 degrees C, but not at 16 degrees C. Delta ces1 Delta ces4 cells display gross defects in cell shape and budding even at permissive temperatures. Functional analysis of CES1 deletion mutants defines a 145 amino acid C-terminal segment of the 915 amino acid Ces1 protein that is necessary and sufficient to complement the Delta ces1 Delta ces 4 cold-**sensitive** phenotype, to restore normal morphology and to suppress the temparature-**sensitive** **mutant** ceg1-25 . A 147 amino acid C-terminal segment of the 942 amino acid Ces4 protein is sufficient to carry out these same functions. Within this carboxyl domain Ces1p and Ces4p are 80% identical to one another. We report isolation of CES1 in a separate **screen** for high copy suppression of a **temperature-sensitive** mutation (A79V) of the **yeast** translation initiation factor Tif1p (eIF-4A). Deletion of the N-terminal 249 amino acids of Ces1p abolished tif1-A79V suppressor function. CES4 on a multicopy plasmid was unable to suppress tif1-A79V . We surmise that whereas the carboxyl domains of Ces1p and Ces4p are functionally redundant in controlling cell morphology and in suppressing ceg1-25 , full-length Ces1p and Ces4p evince distinct genetic interactions that are likely mediated by their N-terminal segments.

L28 ANSWER 28 OF 67 MEDLINE
AN 1998043399 MEDLINE
DN 98043399
TI Mcs4, a two-component system response regulator homologue, regulates the Schizosaccharomyces pombe cell cycle control.
AU Cottarel G
CS Mitotix, Cambridge, Massachusetts 02139, USA.. cottarel@mitotix.com
SO GENETICS, (1997 Nov) 147 (3) 1043-51.
Journal code: FNH. ISSN: 0016-6731.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)

family. Strains carrying the mcs4 and cdc25 mutations display a synthetic osmotic lethal phenotype along with an inability to grow on minimal synthetic medium. These phenotypes are suppressed by a mutation in wee1. In addition, the wis1 gene, encoding a stress-activated mitogen-activated protein kinase kinase, was identified as a dosage suppressor in this **screen**. These findings link the two-component signal transduction system to stress response and cell cycle control in S. pombe.

L28 ANSWER 29 OF 67 MEDLINE
AN 1998038777 MEDLINE
DN 98038777
TI Nucleolar KKE/D repeat proteins Nop56p and Nop58p interact with Nop1p and are required for ribosome biogenesis.
AU Gautier T; Berg`es T; Tollervey D; Hurt E
CS Laboratoire DyOGen, Institut Albert Bonniot, Universite Grenoble I, La Tronche, France.
SO MOLECULAR AND CELLULAR BIOLOGY, (1997 Dec) 17 (12) 7088-98.
Journal code: NGY. ISSN: 0270-7306.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-Y12065
EM 199802
EW 19980204
AB Different point mutations in the nucleolar protein fibrillarin (Nop1p in Saccharomyces cerevisiae) can inhibit different steps in ribosome synthesis. A **screen** for mutations that are synthetically lethal (sl) with the nop1-5 allele, which inhibits pre-rRNA processing, identified NOP56. An independent sl mutation **screen** with nop1-3, which inhibits pre-rRNA methylation, identified a mutation in NOP58. Strikingly, Nop56p and Nop58p are highly homologous (45% identity). Both proteins were found to be essential and localized to the nucleolus. A **temperature-sensitive** lethal **mutant** allele, nop56-2, inhibited many steps in pre-rRNA processing, particularly on the pathway of 25S/5.8S rRNA synthesis, and led to defects in 60S subunit assembly. Epitope-tagged constructs show that both Nop56p and Nop58p are associated with Nop1p in complexes, Nop56p and Nop1p exhibiting a stoichiometric association. These physical interactions presumably underlie the observed sl phenotypes. Well-conserved homologs are present in a range of organisms, including humans (52% identity between human hNop56p and **yeast** Nop56p), suggesting that these complexes have been conserved in evolution.

L28 ANSWER 30 OF 67 MEDLINE
AN 1998028701 MEDLINE
DN 98028701
TI A structure/function analysis of Rat7p/Nup159p, an essential nucleoporin of Saccharomyces cerevisiae.
AU Del Priore V; Heath C; Snay C; MacMillan A; Gorsch L; Dagher S; Cole C
CS Department of Biochemistry, Dartmouth Medical School, Hanover, NH 03755, USA.
NC GM33998 (NIGMS)
CA16038 (NCI)
SO JOURNAL OF CELL SCIENCE, (1997 Dec) 110 (Pt 23) 2987-99.
Journal code: HNK. ISSN: 0021-9533.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199804
EW 19980401
AB Rat7p/Nup159p is an essential nucleoporin of Sac-charomyces cerevisiae originally isolated in a genetic **screen** designed to identify **yeast temperature-sensitive** mutants defective in mRNA export. Here we describe a detailed structural-functional analysis of Rat7p/Nup159p. The mutation in the rat7-1 ts allele, isolated in the original genetic **screen**, was found to be a single base pair change that created a stop codon approximately 100 amino acids upstream of the actual stop codon of this 1,460 amino acid polypeptide, thus eliminating one of the two predicted coiled-coil regions located near the

NPC through its coiled-coil region and adjacent sequences. In addition, we postulate that the N-terminal third of Rat7p/Nup159p plays an important role in mRNA export.

L28 ANSWER 31 OF 67 MEDLINE
AN 97342612 MEDLINE
DN 97342612
TI Interaction between the small GTPase Ran/Gsp1p and Ntf2p is required for nuclear transport.
AU Wong D H; Corbett A H; Kent H M; Stewart M; Silver P A
CS Department of Biological Chemistry and Molecular Pharmacology, Harvard Medical School, Dana-Farber Cancer Institute, Boston, Massachusetts 02115, USA.
SO MOLECULAR AND CELLULAR BIOLOGY, (1997 Jul) 17 (7) 3755-67.
Journal code: NGY. ISSN: 0270-7306.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199709
AB Bidirectional movement of proteins and RNAs across the nuclear envelope requires Ran, a Ras-like GTPase. A genetic **screen** of the **yeast** Saccharomyces cerevisiae was performed to isolate conditional alleles of GSP1, a gene that encodes a homolog of Ran. Two **temperature-sensitive** alleles, gsp1-1 and gsp1-2, were isolated. The mutations in these two alleles map to regions that are structurally conserved between different members of the Ras family. Each **mutant** strain exhibits various nuclear transport defects. Both biochemical and genetic experiments indicate a decreased interaction between Ntf2p, a factor which is required for protein import, and the **mutant** GSP1 gene products. Overexpression of NTF2 can suppress the **temperature sensitive** phenotype of gsp1-1 and gsp1-2 and partially rescue nuclear transport defects. However, overexpression of a **mutant** allele of NTF2 with decreased binding to Gsp1p cannot rescue the **temperature** sensitivity of gsp1-1 and gsp1-2. Taken together, these data demonstrate that the interaction between Gsp1p and Ntf2p is critical for nuclear transport.

L28 ANSWER 32 OF 67 MEDLINE
AN 97327760 MEDLINE
DN 97327760
TI Fission **yeast** dim1(+) encodes a functionally conserved polypeptide essential for mitosis.
AU Berry L D; Gould K L
CS Howard Hughes Medical Institute, Department of Cell Biology, Vanderbilt University, Nashville, Tennessee 37212, USA.
NC GM47728 (NIGMS)
SO JOURNAL OF CELL BIOLOGY, (1997 Jun 16) 137 (6) 1337-54.
Journal code: HMV. ISSN: 0021-9525.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Cancer Journals; Priority Journals
OS GENBANK-AF001214
EM 199709
AB In a **screen** for second site mutations capable of reducing the restrictive **temperature** of the fission **yeast** **mutant** cdc2-D217N, we have isolated a novel **temperature-sensitive mutant**, dim1-35. When shifted to restrictive **temperature**, dim1-35 **mutant** cells arrest before entry into mitosis or proceed through mitosis in the absence of nuclear division, demonstrating an uncoupling of proper DNA segregation from other cell cycle events. Deletion of dim1 from the Schizosaccharomyces pombe genome produces a lethal G2 arrest phenotype. Lethality is rescued by overexpression of the mouse dim1 homolog, mdim1. Likewise, deletion of the Saccharomyces cerevisiae dim1 homolog, CDH1, is lethal. Both mdim1 and dim1(+) are capable of rescuing lethality in the cdh1::HIS3 **mutant**. Although dim1-35 displays no striking genetic interactions with various

TI Saccharomyces cerevisiae cell lysis mutations cly5 and cly7 define **temperature-sensiti** alleles of PKC1, the gene enco**ng** **yeast** protein kinas**e** C.
AU Baymiller J; McCullough J E
CS Department of Microbial Molecular Biology, Bristol Myers Squibb Pharmaceutical Research Institute, Princeton, NJ 08543, USA.
SO YEAST, (1997 Mar 30) 13 (4) 305-12.
Journal code: YEA. ISSN: 0749-503X.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199709
EW 19970904
AB A set of **temperature-sensitive** Saccharomyces cerevisiae mutants designated cly (for cell lysis) 1-8 because the cells lyse at high **temperature** was isolated in a large **screen** for **yeast temperature-sensitive** (Hartwell, 1967). Here we report the isolation of two plasmids, containing inserts that both the cly5 and cly7 mutations. DNA sequencing revealed that both of these inserts contain the gene encoding **yeast** protein kinase C (PKC1) (Levin et al., 1990). Sequencing of the **mutant** alleles revealed that cly5 and cly7 contain distinct mutations separated by 194 base pairs. Consistent with this, the cly5 and cly7 ts alleles do not complement each other, and they are genetically linked to PKC1 and to each other. Like other **temperature-sensitive** pkc1 alleles, the **temperature-sensitive** phenotype is eliminated by growth in high osmotic strength media (Levin and Bartlett-Heubusch, 1992).

L28 ANSWER 34 OF 67 MEDLINE
AN 97154527 MEDLINE
DN 97154527
TI C-terminal truncations of the **yeast** nucleoporin Nup145p produce a rapid **temperature**-conditional mRNA export defect and alterations to nuclear structure [published erratum appears in Mol Cell Biol 1997 Apr;17(4):2347-50].
AU Dockendorff T C; Heath C V; Goldstein A L; Snay C A; Cole C N
CS Department of Biochemistry, Dartmouth Medical School, Hanover, New Hampshire 03755, USA.
NC CA09658 (NCI)
CA16038 (NCI)
GM33998 (NIGMS)
SO MOLECULAR AND CELLULAR BIOLOGY, (1997 Feb) 17 (2) 906-20.
Journal code: NGY. ISSN: 0270-7306.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199704
AB A **screen** for **temperature-sensitive** mutants of Saccharomyces cerevisiae defective in nucleocytoplasmic trafficking of poly(A)+ RNA has identified an allele of the NUP145 gene, which encodes an essential nucleoporin. NUP145 was previously identified by using a genetic synthetic lethal **screen** (E. Fabre, W. C. Boelens, C. Wimmer, I. W. Mattaj, and E. C. Hurt, Cell 78:275-289, 1994) and by using a monoclonal antibody which recognizes the GLFG family of vertebrate and **yeast** nucleoporins (S. R. Wente and G. Blobel, J. Cell Biol. 125:955-969, 1994). Cells carrying the new allele, nup145-10, grew at 23 and 30 degrees C but were unable to grow at 37 degrees C. Many cells displayed a modest accumulation of poly(A)+ RNA under permissive growth conditions, and all cells showed dramatic and rapid nuclear accumulation of poly(A)+ RNA following a shift to 37 degrees C. The **mutant** allele contains a nonsense codon which truncates the 1,317-amino-acid protein to 698 amino acids. This prompted us to examine the role of the carboxyl half of Nup145p. Several additional alleles that encode C-terminally truncated proteins or proteins containing internal deletions of portions of the carboxyl half of Nup145p were constructed. Analysis of these mutants indicates that some sequences between amino acids 698 and 1095 are essential for RNA export and for growth at 37 degrees C. In

reduction in the level of synthesis of rRNAs to approximately 25% of the wild-type level.

L28 ANSWER 35 OF 67 MEDLINE
AN 97148198 MEDLINE
DN 97148198
TI Mutations that suppress the thermosensitivity of green fluorescent protein.
AU Siemering K R; Golbik R; Sever R; Haseloff J
CS MRC Laboratory of Molecular Biology, Cambridge, UK.
SO CURRENT BIOLOGY, (1996 Dec 1) 6 (12) 1653-63.
Journal code: B44. ISSN: 0960-9822.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-U87973; GENBANK-U87974
EM 199705
AB BACKGROUND: The green fluorescent protein (GFP) of the jellyfish Aequorea victoria has recently attracted great interest as the first example of a cloned reporter protein that is intrinsically fluorescent. Although successful in some organisms, heterologous expression of GFP has not always been straight forward. In particular, expression of GFP in cells that require incubation temperatures around 37 degrees C has been problematic. RESULTS: We have carried out a **screen** for **mutant** forms of GFP that fluoresce more intensely than the wild-type protein when expressed in E. coli at 37 degrees C. We have characterized a bright **mutant** (GFPA) with reduced sensitivity to **temperature** in both bacteria and **yeast**, and have shown that the amino acids substituted in GFPA act by preventing **temperature**-dependent misfolding of the GFP apoprotein. We have shown that the excitation and emission spectra of GFPA can be manipulated by site-directed mutagenesis without disturbing its improved folding characteristics, and have produced a thermostable folding **mutant** (GFP5) that can be efficiently excited using either long-wavelength ultraviolet or blue light. Expression of GFP5 results in greatly improved levels of fluorescence in both microbial and mammalian cells cultured at 37 degrees C. CONCLUSIONS: The thermotolerant mutants of GFP greatly improve the sensitivity of the protein as a visible reporter molecule in bacterial, **yeast** and mammalian cells. The fluorescence spectra of these mutants can be manipulated by further mutagenesis without deleteriously affecting their improved folding characteristics, so it may be possible to engineer a range of spectral variants with improved tolerance to **temperature**. Such a range of **sensitive** reporter proteins will greatly improve the prospects for GFP-based applications in cells that require relatively high incubation temperatures.

L28 ANSWER 36 OF 67 MEDLINE
AN 97133420 MEDLINE
DN 97133420
TI A novel fluorescence-activated cell sorter-based **screen** for **yeast** endocytosis mutants identifies a **yeast** homologue of mammalian eps15.
AU Wendland B; McCaffery J M; Xiao Q; Emr S D
CS Division of Cellular and Molecular Medicine, University of California at San Diego, School of Medicine, La Jolla 92093-0668, USA.
NC GM32703 (NIGMS)
CA58689 (NCI)
SO JOURNAL OF CELL BIOLOGY, (1996 Dec) 135 (6 Pt 1) 1485-500.
Journal code: HMV. ISSN: 0021-9525.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199703
EW 19970304
AB A complete understanding of the molecular mechanisms of endocytosis requires the discovery and characterization of the protein machinery that mediates this aspect of membrane trafficking. A novel genetic **screen** was used to identify **yeast** mutants defective in internalization of bulk lipid. The fluorescent lipophilic styryl dye FM4-64 was used in conjunction with FACS to enrich for **yeast**

with the mammalian clathrin adaptor-associated protein, eps15. Both proteins contain multiple EH (eps15 homology) domains, a motif proposed to mediate protein-protein interactions. Phalloidin labeling of filamentous actin revealed profound defects in the actin cytoskeleton in both dim mutants. EM analysis revealed that the dim mutants accumulate vesicles and tubulo-vesicular structures reminiscent of mammalian early endosomes. In addition, the accumulation of novel plasma membrane invaginations where endocytosis is likely to occur were visualized in the mutants by electron microscopy using cationized ferritin as a marker for the endocytic pathway. This new screening strategy demonstrates a role for She4p and Pan1p in endocytosis, and provides a new general method for the identification of additional endocytosis mutants.

L28 ANSWER 37 OF 67 MEDLINE
AN 97015885 MEDLINE
DN 97015885
TI A connection between pre-mRNA splicing and the cell cycle in fission **yeast**: cdc28+ is allelic with prp8+ and encodes an RNA-dependent ATPase/helicase.
AU Lundgren K; Allan S; Urushiyama S; Tani T; Ohshima Y; Frendewey D; Beach D
CS Howard Hughes Medical Institute, Cold Spring Harbor Laboratory, New York 11724, USA.
NC GM-34607 (NIGMS)
SO MOLECULAR BIOLOGY OF THE CELL, (1996 Jul) 7 (7) 1083-94.
Journal code: BAU. ISSN: 1059-1524.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-U48733
EM 199702
AB The fission-**yeast** gene cdc28+ was originally identified in a **screen** for **temperature-sensitive** mutants that exhibit a cell-division cycle arrest and was found to be required for mitosis. We undertook a study of this gene to understand more fully the general requirements for entry into mitosis. Cells carrying the conditional lethal cdc28-P8 mutation divide once and arrest in G2 after being shifted to the restrictive **temperature**. We cloned the cdc28+ gene by complementation of the **temperature-sensitive** growth arrest in cdc28-P8. DNA sequence analysis indicated that cdc28+ encodes a member of the DEAH-box family of putative RNA-dependent ATPases or helicases. The Cdc28 protein is most similar to the Prp2, Prp16, and Prp22 proteins from budding **yeast**, which are required for the splicing of mRNA precursors. Consistent with this similarity, the cdc28-P8 **mutant** accumulates unspliced precursors at the restrictive **temperature**. Independently, we isolated a **temperature-sensitive** pre-mRNA splicing **mutant** prp8-1 that exhibits a cell-cycle phenotype identical to that of cdc28-P8.
We have shown that cdc28 and prp8 are allelic. These results suggest a connection between pre-mRNA splicing and progression through the cell cycle.

L28 ANSWER 38 OF 67 MEDLINE
AN 96431716 MEDLINE
DN 96431716
TI Isolation and characterization of fission **yeast** mutants defective in the assembly and placement of the contractile actin ring.
AU Chang F; Woollard A; Nurse P
CS Imperial Cancer Research Fund, London, UK.
SO JOURNAL OF CELL SCIENCE, (1996 Jan) 109 (Pt 1) 131-42.
Journal code: HNK. ISSN: 0021-9533.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199702
EW 19970204
AB Fission **yeast** cells divide by medial cleavage using an actin-based contractile ring. We have conducted a genetic **screen**

the nucleus is positioned normally, indicating that the mid1 gene product is required to couple the division site to the position of the nucleus. mid1 **mutant** cells may reveal a new cell cycle checkpoint in telophase that coordinates cell division and the proper distribution of nuclei. The actin ring forms medially in a beta-tubulin **mutant**, showing that actin ring formation and placement are not dependent on the mitotic spindle.

L28 ANSWER 39 OF 67 MEDLINE
AN 96413887 MEDLINE
DN 96413887
TI CDNA cloning of p112, the largest regulatory subunit of the human 26s proteasome, and functional analysis of its **yeast** homologue, sen3p.
AU Yokota K; Kagawa S; Shimizu Y; Akioka H; Tsurumi C; Noda C; Fujimuro M; Yokosawa H; Fujiwara T; Takahashi E; Ohba M; Yamasaki M; DeMartino G N; Slaughter C A; Toh-e A; Tanaka K
CS Department of Urology, School of Medicine, Tokushima, Japan.
NC DK-46181 (NIDDK)
SO MOLECULAR BIOLOGY OF THE CELL, (1996 Jun) 7 (6) 853-70.
Journal code: BAU. ISSN: 1059-1524.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-D44466
EM 199703
EW 19970304
AB The 26S proteasome is a large multisubunit protease complex, the largest regulatory subunit of which is a component named p112. Molecular cloning of cDNA encoding human p112 revealed a polypeptide predicted to have 953 amino acid residues and a molecular mass of 105,865. The human p112 gene was mapped to the q37.1-q37.2 region of chromosome 2. Computer analysis showed that p112 has strong similarity to the Saccharomyces cerevisiae Sen3p, which has been listed in a gene bank as a factor affecting tRNA splicing endonuclease. The SEN3 also was identified in a synthetic lethal **screen** with the nin1-1 **mutant**, a **temperature-sensitive mutant** of NIN1. NIN1 encodes p31, another regulatory subunit of the 26S proteasome, which is necessary for activation of Cdc28p kinase. Disruption of the SEN3 did not affect cell viability, but led to **temperature-sensitive** growth. The human p112 cDNA suppressed the growth defect at high **temperature** in a SEN3 disruptant, indicating that p112 is a functional homologue of the **yeast** Sen3p. Maintenance of SEN3 disruptant cells at the restrictive **temperature** resulted in a variety of cellular dysfunctions, including defects in proteolysis mediated by the ubiquitin pathway, in the N-end rule system, in the stress response upon cadmium exposure, and in nuclear protein transportation. The functional abnormality induced by SEN3 disruption differs considerably from various phenotypes shown by the nin1-1 mutation, suggesting that these two regulatory subunits of the 26S proteasome play distinct roles in the various processes mediated by the 26S proteasome.

L28 ANSWER 40 OF 67 MEDLINE
AN 96293355 MEDLINE
DN 96293355
TI The Saccharomyces cerevisiae actin-related protein Arp2 is involved in the actin cytoskeleton.
AU Moreau V; Madania A; Martin R P; Winson B
CS Institut de Biologie Moleculaire et Cellulaire du C.N.R.S. U.P.R. 9005, Strasbourg, France.
SO JOURNAL OF CELL BIOLOGY, (1996 Jul) 134 (1) 117-32.
Journal code: HMV. ISSN: 0021-9525.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199611
IT Arp2 is an essential yeast actin-related protein. Disruption of

of Arp2p in the actin cytoskeleton. Random budding patterns were observed in both haploid and diploid arp2-H330L **mutant** cells. Endocytosis, as judged by Lucifer yellow uptake, was severely reduced in the **mutant**, at all temperatures. In addition, genetic interaction was observed between **temperature-sensitive** alleles arp2-H330L and cdc10-1. CDC10 is a gene encoding a neck filament-associated protein that is necessary for polarized growth and cytokinesis. Overall, the immunolocalization, **mutant** phenotypes, and genetic interaction suggest that the Arp2 protein is an essential component of the actin cytoskeleton that is involved in membrane growth and polarity, as well as in endocytosis.

L28 ANSWER 41 OF 67 MEDLINE
AN 96279259 MEDLINE
DN 96279259
TI Mutation of the Rab6 homologue of Saccharomyces cerevisiae, YPT6, inhibits both early Golgi function and ribosome biosynthesis.
AU Li B; Warner J R
CS Department of Cell Biology, Albert Einstein College of Medicine, Bronx, New York 10461, USA.
NC GM 25532 (NIGMS)
CA13330 (NCI)
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1996 Jul 12) 271 (28) 16813-9.
Journal code: HIV. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199610
AB A **screen** was designed to identify **temperature-sensitive** mutants of Saccharomyces cerevisiae, whose transcription of both ribosomal RNA and ribosomal protein genes is repressed at the nonpermissive **temperature**. The gene from one such **mutant** was cloned by complementation. The gene encodes a predicted product that is nearly 65% identical to the human GTPase, Rab6, and is likely to be identical to the **yeast** gene YPT6. It is essential for growth only at elevated temperatures. The **mutant** strain is partially defective in the maturation of the vacuolar protein carboxypeptidase Y, as well as in the secretion of invertase, which accumulates as a core-glycosylated form characteristic of the endoplasmic reticulum or the cis-Golgi, suggesting that Ypt6p is involved in an early step of the secretory pathway, earlier than that reported for the mammalian Rab6. The **mutant** protein, a truncation at codon 64 of 215, has a stronger phenotype than the null allele of YPT6. Four other mutants selected for defective ribosome synthesis at the nonpermissive **temperature** were also found to have defects in carboxypeptidase Y maturation, giving emphasis to our previous finding that a functional secretory pathway is essential for continued ribosome synthesis. Cloning of extragenic suppressors of the ts allele of YPT6 has revealed two additional proteins that influence the secretory pathway: Ssd1p, a suppressor of many mutations, and Imh1p, which bears some homology to the C-terminal portion of the cytoskeletal proteins integrin and myosin.

L28 ANSWER 42 OF 67 MEDLINE
AN 96239540 MEDLINE
DN 96239540
TI Characterization of an essential Orc2p-associated factor that plays a role in DNA replication.
AU Hardy C F
CS Department of Cell Biology and Physiology, Washington University School of Medicine, St Louis, Missouri 63110, USA.
SO MOLECULAR AND CELLULAR BIOLOGY, (1996 Apr) 16 (4) 1832-41.
Journal code: NGY. ISSN: 0270-7306.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-U48888

element. These results suggest a role for OAFI in the initiation of DNA replication. **Mutan**[redacted]lleles of cdc7 and cdc14 were a[redacted]o isolated in the orc2-1 synthetic lethal **screen**. Cdc7p, like C[redacted]1p, also interacts with Orc2p in two-hybrid assays.

L28 ANSWER 43 OF 67 MEDLINE
AN 96228684 MEDLINE
DN 96228684
TI SCD5, a suppressor of clathrin deficiency, encodes a novel protein with a late secretory function in **yeast**.
AU Nelson K K; Holmer M; Lemmon S K
CS Department of Molecular Biology and Microbiology, Case Western Reserve University School of Medicine, Cleveland, Ohio 44106-4960, USA.
NC HL-07415 (NHLBI)
SO MOLECULAR BIOLOGY OF THE CELL, (1996 Feb) 7 (2) 245-60.
Journal code: BAU. ISSN: 1059-1524.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-U03492
EM 199610
AB Clathrin and its associated proteins constitute a major class of coat proteins involved in vesicle budding during membrane transport. An interesting characteristic of the **yeast** clathrin heavy chain gene (CHC1) is that in some strains a CHC1 deletion is lethal, while in others it is not. Recently, our laboratory developed a **screen** that identified five multicopy suppressors that can rescue lethal strains of clathrin heavy chain-deficient **yeast** (Chc - scd1-i) to viability. One of these suppressors, SCD5, encodes a novel protein of 872 amino acids containing two regions of repeated motifs of unknown function.
Deletion of SCD5 has shown that it is essential for cell growth at 30 degrees C. scd5-delta strains carrying low copy plasmids encoding C-terminal truncations of Scd5p are **temperature sensitive** for growth at 37 degrees C. At the nonpermissive **temperature**, cells expressing a 338-amino acid deletion (Scd5P-delta 338) accumulate an internal pool of fully glycosylated invertase and mature alpha-factor, while processing and sorting of the vacuolar hydrolase carboxypeptidase Y is normal. The truncation **mutant** also accumulates 80- to 100-nm vesicles similar to many late sec mutants. Moreover, at 34 degrees C, overexpression of Scd5p suppresses the **temperature** sensitivity of a sec2 **mutant**, which is blocked at a post-Golgi step of the secretory pathway. Biochemical analyses indicate that approximately 50% of Scd5p sediments with a 100,000 x g membrane fraction and is associated as a peripheral membrane protein. Overall, these results indicate that Scd5p is involved in vesicular transport at a late stage of the secretory pathway. Furthermore, this suggests that the lethality of clathrin-deficient **yeast** can be rescued by modulation of vesicular transport at this late secretory step.

L28 ANSWER 44 OF 67 MEDLINE
AN 96181092 MEDLINE
DN 96181092
TI Pds1p is required for faithful execution of anaphase in the **yeast**, Saccharomyces cerevisiae.
AU Yamamoto A; Guacci V; Koshland D
CS Carnegie Institution of Washington, Department of Embryology, Baltimore, Maryland 21210, USA.
NC GM41718 (NIGMS)
SO JOURNAL OF CELL BIOLOGY, (1996 Apr) 133 (1) 85-97.
Journal code: HMV. ISSN: 0021-9525.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
OS GENBANK-U12185
EM 199607
AB To identify mutations that cause defects in mitosis, a collection of mutants in Saccharomyces cerevisiae was screened by a rapid visual assay for abnormal chromosome segregation. From this **screen** we [redacted] pds1-1 that was independently identified in an

elongation pds1 mutants undergo cytokinesis, leading to the missegregation of both chromosomes and spindle pole bodies. After a normal cell division pds1-1 mutants also initiate new rounds of DNA replication, spindle pole body duplication, and bud formation. Thus, in the pds1-1 **mutant** at 37 degrees C, cell cycle progression is uncoupled from the completion of anaphase. A pds1 deletion allele has similar phenotypes to the original allele. Taken together these results suggest that Pds1 protein plays an important role in chromosome segregation at 23 degrees C and an essential role for this process at 37 degrees C. The PDS1 gene encodes a novel 42-kD nuclear protein that has both basic and acidic domains. The level of PDS1 mRNA varies with the cell cycle with maximal accumulation around the G1/S boundary. The stability of Pds1 protein also appears to change during the cell cycle as overproduced Pds1p is stable in S and M but degraded in early G1. Therefore, expression of Pds1p is regulated apparently both transcriptionally and postranslationally during the cell cycle. The phenotypes of pds1 mutants and expression pattern of Pds1p are discussed in the context of other spindle-defective mutants and the knowledge that Pds1 protein is an inhibitor of anaphase (Yamamoto, T.J., G. Li, B. Schaar, I. Szilak, and D.W. Cleveland. 1992. Nature (Lond.). 359:536-539).

L28 ANSWER 45 OF 67 MEDLINE
AN 96164183 MEDLINE
DN 96164183
TI BET3 encodes a novel hydrophilic protein that acts in conjunction with **yeast** SNAREs.
AU Rossi G; Kolstad K; Stone S; Palluault F; Ferro-Novick S
CS Department of Cell Biology, Yale University School of Medicine, New Haven, Connecticut 06510, USA.
NC 1 RO1 GM-45431 (NIGMS)
CA-46128 (NCI)
SO MOLECULAR BIOLOGY OF THE CELL, (1995 Dec) 6 (12) 1769-80.
Journal code: BAU. ISSN: 1059-1524.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199606
AB Here we report the identification of BET3, a new member of a group of interacting genes whose products have been implicated in the targeting and fusion of endoplasmic reticulum (ER) to Golgi transport vesicles with their acceptor compartment. A **temperature-sensitive mutant** in bet3-1 was isolated in a synthetic lethal **screen** designed to identify new genes whose products may interact with BET1, a type II integral membrane protein that is required for ER to Golgi transport. At 37 degrees C, bet3-1 fails to transport invertase, alpha-factor, and carboxypeptidase Y from the ER to the Golgi complex. As a consequence, this **mutant** accumulates dilated ER and small vesicles. The SNARE complex, a docking/fusion complex, fails to form in this **mutant**. Furthermore, BET3 encodes an essential 22-kDa hydrophilic protein that is conserved in evolution, which is not a component of this complex. These findings support the hypothesis that Bet3p may act before the assembly of the SNARE complex.

L28 ANSWER 46 OF 67 MEDLINE
AN 96154047 MEDLINE
DN 96154047
TI CUS1, a suppressor of cold-**sensitive** U2 snRNA mutations, is a novel **yeast** splicing factor homologous to human SAP 145.
AU Wells S E; Neville M; Haynes M; Wang J; Igel H; Ares M Jr
CS Biology Department, Sinsheimer Laboratories, University of California, Santa Cruz 95064, USA.
NC GM40478 (NIGMS)
SO GENES AND DEVELOPMENT, (1996 Jan 15) 10 (2) 220-32.
Journal code: FN3. ISSN: 0890-9369.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)

spliceosome. The suppressor protein rescues the spliceosome assembly defect of the **mutant** U2 in vitro, indicating that suppression is direct. Allele specificity tests show that the suppressor does not simply bypass the requirement for U2 stem loop IIa. Extra copies of wild-type CUS1, but not CUS1-54, suppress the **temperature-sensitive** prp11 and prp5 mutations, linking CUS1 protein to a subset of other factors required at the same step of spliceosome assembly.
CUS1 is homologous to SAP 145, a component of the mammalian U2 snRNP that interacts with pre-mRNA. The **yeast** genome also encodes a homolog of human SAP 49, a protein that interacts strongly with both SAP 145 and pre-mRNA, underscoring the conservation of U2 snRNP proteins that function in spliceosome assembly.

L28 ANSWER 47 OF 67 MEDLINE
AN 96134020 MEDLINE
DN 96134020
TI Nuclear pore complex clustering and nuclear accumulation of poly(A)+ RNA associated with mutation of the Saccharomyces cerevisiae RAT2/NUP120 gene.
AU Heath C V; Copeland C S; Amberg D C; Del Priore V; Snyder M; Cole C N
CS Department of Biochemistry, Dartmouth Medical School, Hanover, New Hampshire 03755, USA.
NC GM33998 (NIGMS)
GM36494 (NIGMS)
CA16038 (NCI)
SO JOURNAL OF CELL BIOLOGY, (1995 Dec) 131 (6 Pt 2) 1677-97.
Journal code: HMV. ISSN: 0021-9525.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
OS GENBANK-Z28057
EM 199605
AB To identify genes involved in the export of messenger RNA from the nucleus to the cytoplasm, we used an in situ hybridization assay to **screen** **temperature-sensitive** strains of Saccharomyces cerevisiae. This identified those which accumulated poly(A)+ RNA in their nuclei when shifted to the non-permissive **temperature** of 37 degrees C. We describe here the properties of **yeast** strains carrying mutations in the RAT2 gene (RAT - ribonucleic acid trafficking) and the cloning of the RAT2 gene. Only a low percentage of cells carrying the rat2-1 allele showed nuclear accumulation of poly(A)+ RNA when cultured at 15 degrees or 23 degrees C, but within 4 h of a shift to the nonpermissive **temperature** of 37 degrees C, poly(A)+ RNA accumulated within the nuclei of approximately 80% of cells. No defect was seen in the nuclear import of a reporter protein bearing a nuclear localization signal. Nuclear pore complexes (NPCs) are distributed relatively evenly around the nuclear envelope in wild-type cells. In cells carrying either the rat2-1 or rat2-2 allele, NPCs were clustered together into one or a few regions of the nuclear envelope. This clustering was a constitutive property of **mutant** cells. NPCs remained clustered in crude nuclei isolated from **mutant** cells, indicating that these clusters are not able to redistribute around the nuclear envelope when nuclei are separated from cytoplasmic components. Electron microscopy revealed that these clusters were frequently found in a protuberance of the nuclear envelope and were often located close to the spindle pole body. The RAT2 gene encodes a 120-kD protein without similarity to other known proteins. It was essential for growth only at 37 degrees C, but the growth defect at high **temperature** could be suppressed by growth of **mutant** cells in the presence of high osmolarity media containing 1.0 M sorbitol or 0.9 M NaCl. The phenotypes seen in cells carrying a disruption of the RAT2 gene were very similar to those seen with the rat2-1 and rat2-2 alleles. Epitope tagging was used to show that Rat2p is located at the nuclear periphery and co-localizes with **yeast** NPC proteins recognized by the RL1 monoclonal antibody. The rat2-1 allele was synthetically lethal with both the rat3-1/nup133-1 and rat7-1/nup159-1 alleles. These results indicate that the product of this

DK-35187 (NIDDK)
+
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1995 Sep 1) 270 (35) 20643-52.
Journal code: HIV. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199512
AB As a first step toward identifying the important structural elements of calmodulin from Schizosaccharomyces pombe, we examined the ability of heterologous calmodulins and Ca(2+)-binding site **mutant** S. pombe calmodulins to replace the essential cam1+ gene. A cDNA encoding vertebrate calmodulin allows growth of S. pombe. However, calmodulin from Saccharomyces cerevisiae does not support growth even though the protein is produced at high levels. With one exception, all **mutant** S. pombe calmodulins with one or more intact Ca(2+)-binding sites allow growth at 21 degrees C. A **mutant** containing only an intact Ca(2+)-binding site 3 fails to support growth, as does S. pombe calmodulin with all four Ca(2+)-binding sites mutated. Several of the **mutant** proteins confer a **temperature-sensitive** phenotype. Analysis of the degree of **temperature** sensitivity allows the Ca(2+)-binding sites to be ranked by their ability to support fission **yeast** proliferation. Site 2 is more important than site 1, which is more important than site 4, which is more important than site 3. A visual colony color **screen** based on the fission **yeast** ade1+ gene was developed to perform these genetic analyses. To compare the Ca(2+)-binding properties of individual sites to their functional importance for viability, Ca2+ binding to calmodulin from S. pombe was studied by 1H NMR spectroscopy. NMR analysis indicates a Ca(2+)-binding profile that differs from those previously determined for vertebrate and S. cerevisiae calmodulins. Ca(2+)-binding site 3 has the highest relative affinity for Ca2+, while the affinities of sites 1, 2, and 4 are indistinguishable. A combination of an in vivo functional assay and an in vitro physical assay reveals that the relative affinity of a site for Ca2+ does not predict its functional importance.

L28 ANSWER 49 OF 67 MEDLINE
AN 95292334 MEDLINE
DN 95292334
TI ORC and Cdc6p interact and determine the frequency of initiation of DNA replication in the genome.
AU Liang C; Weinreich M; Stillman B
CS Cold Spring Harbor Laboratory, New York 11724, USA.
NC AI20460 (NIAID)
SO CELL, (1995 Jun 2) 81 (5) 667-76.
Journal code: CQ4. ISSN: 0092-8674.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199509
AB The origin recognition complex (ORC) binds replicators in the **yeast** S. cerevisiae in a manner consistent with it being an initiator protein for DNA replication. Two-dimensional (2D) gel techniques were used to examine directly initiation of chromosomal DNA replication in **temperature-sensitive** orc mutants. Unlike in wild-type cells, in orc2-1 and orc5-1 **mutant** cells, only a subset of replicators formed active origins of DNA replication at the permissive **temperature**. At the restrictive **temperature**, the number of active replicators was diminished further. Using a genetic **screen**, CDC6 was identified as a multicopy suppressor of orc5-1. 2D gel and biochemical analyses demonstrated that Cdc6p interacted functionally and physically with ORC. We suggest that ORC and Cdc6p form a prereplication complex at individual replicators and therefore cooperate to determine the frequency of initiation of DNA replication in the

SO JOURNAL OF CELL BIOLOGY, (1995 May) 129 (4) 939-55.
Journal code: HMV. SN: 0021-9525.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
OS GENBANK-L40634
EM 199508
AB In a **screen** for Saccharomyces cerevisiae genes required for nucleocytoplasmic transport of messenger RNA, we identified the RAT7 gene (ribonucleic acid trafficking), which encodes an essential protein of 1,460 amino acids. Rat7p is located at the nuclear rim in a punctate pattern characteristic of nucleoporins. Furthermore, the central third of Rat7p contains 22 XXFG and three XFXFG degenerate repeats that are similar to signature GLFG and XFXFG repeats present in a majority of **yeast** and some mammalian nucleoporins sequenced to date. Shift of a strain bearing the **temperature-sensitive** rat7-1 allele from 23 degrees C to 37 degrees C resulted in rapid (within 15 minutes) cessation of mRNA export, but did not cause concomitant cytoplasmic accumulation of a reporter protein bearing a nuclear localization signal. This suggests that Rat7p may play a direct role in nucleocytoplasmic export of RNA. Immunofluorescence and thin section electron microscopy revealed that in rat7-1 cells grown at 23 degrees C, the majority of nuclear pore complexes (NPCs) were clustered on one side of the nucleus. No ultrastructural abnormalities of the nuclear envelope were seen. Interestingly, shifting rat7-1 cells to 37 degrees C for 1 h caused the NPCs to disperse, restoring near wild-type NPC distribution. After this **temperature** shift, the **mutant** Rat7p was no longer detectable by immunofluorescence.

L28 ANSWER 51 OF 67 MEDLINE
AN 95249592 MEDLINE
DN 95249592
TI A simple p53 functional assay for screening cell lines, blood, and tumors.
AU Flaman J M; Frebourg T; Moreau V; Charbonnier F; Martin C; Chappuis P; Sappino A P; Limacher I M; Bron L; Benhattar J; et al
CS Unite de Genetique Moleculaire, Centre Hospitalier, Universitaire de Rouen, France..
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1995 Apr 25) 92 (9) 3963-7.
Journal code: PV3. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199508
AB Mutations in the p53 gene are implicated in the pathogenesis of half of all human tumors. We have developed a simple functional assay for p53 mutation in which human p53 expressed in Saccharomyces cerevisiae activates transcription of the ADE2 gene. Consequently, **yeast** colonies containing wild-type p53 are white and colonies containing **mutant** p53 are red. Since this assay tests the critical biological function of p53, it can distinguish inactivating mutations from functionally silent mutations. By combining this approach with gap repair techniques in which unpurified p53 reverse transcription-PCR products are cloned by homologous recombination in vivo it is possible to **screen** large numbers of samples and multiple clones per sample for biologically important mutations. This means that mutations can be detected in tumor specimens contaminated with large amounts of normal tissue. In addition, the assay detects **temperature-sensitive** mutants, which give pink colonies. We show here that this form of p53 functional assay can be used rapidly to detect germline mutations in blood samples, somatic mutations in tumors, and mutations in cell lines.

L28 ANSWER 52 OF 67 MEDLINE
AN 95203678 MEDLINE
DN 95203678
TI CHL12, a gene essential for the fidelity of chromosome transmission in the

chromosome III and circular centromeric plasmids. A genomic clone of CHL12
was isolated and used to map its physical position on the right arm of chromosome XIII near the ADH3 locus. Nucleotide sequence analysis of CHL12
revealed a 2.2-kb open reading frame with a 84-kD predicted protein sequence. Analysis of the sequence upstream of the CHL12 open reading frame revealed the presence of two imperfect copies of MluI motif, ACGCGT,
a sequence associated with many DNA metabolism genes in **yeast**. Analysis of the amino acid sequence revealed that the protein contains a NTP-binding domain and shares a low degree of homology with subunits of replication factor C (RF-C). A strain containing a null allele of CHL12 was viable under standard growth conditions, and as well as original mutants exhibited an increase in the level of spontaneous mitotic recombination, slow growth and cold-**sensitive** phenotypes. Most of cells carrying the null chl12 mutation arrested as large budded cells with the nucleus in the neck at nonpermissive **temperature** that typical for cell division cycle (cdc) mutants that arrest in the cell cycle at a point either immediately preceding M phase or during S phase. Cell cycle arrest of the chl12 **mutant** requires the RAD9 gene. We conclude that the CHL12 gene product has critical role in DNA metabolism.

L28 ANSWER 53 OF 67 MEDLINE
AN 95050267 MEDLINE
DN 95050267
TI Isolation and characterization of point mutations in the Escherichia coli grpE heat shock gene.
AU Wu B; Ang D; Snavely M; Georgopoulos C
CS Department of Cellular, Viral and Molecular Biology, University of Utah School of Medicine, Salt Lake City 84132..
NC AI21029 (NIAID)
SO JOURNAL OF BACTERIOLOGY, (1994 Nov) 176 (22) 6965-73.
Journal code: HH3. ISSN: 0021-9193.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199502
AB The Escherichia coli grpE gene (along with dnaK, dnaJ, groEL, and groES) was originally identified as one of the host factors required for phage lambda growth. The classical grpE280 mutation was the only grpE mutation that resulted from the initial **screen** and shown to specifically block the initiation of lambda DNA replication. Here we report the isolation of several new grpE missense mutations, again using phage lambda
resistance as a selection. All mutants fall into two groups based on their
temperature-dependent phenotype for lambda growth. Members of the first group (I), including grpE17 and grpE280, which was obtained again, are resistant to lambda growth at both 30 and 42 degrees C. Members of the
second group (II), including grpE25, grpE66, grpE103, grpE13a, grpE57b, and grpE61, are **sensitive** to lambda growth at 30 degrees C but resistant at 42 degrees C. All mutations are recessive, since an E. coli grpE null **mutant** strain carrying these **mutant** alleles on low-copy-number plasmids are **sensitive** to infection by the lambda grpE+ transducing phage. Both group I and group II mutants are **temperature sensitive** for E. coli growth above 42 degrees C. The nucleotide changes were identified by sequencing analyses and shown to be dispersed throughout the latter 75% of the grpE coding region. Most of the amino acid changes occur at conserved residues, as judged by sequence comparisons between E. coli and other bacterial and **yeast** GrpE homologs. The isolation of these new mutations is the first step toward a structure-function analysis of the GrpE protein.

L28 ANSWER 54 OF 67 MEDLINE
AN 94193698 MEDLINE
DN 94193698
TI A conditionally lethal **yeast mutant** blocked at the first step in glycosyl phosphatidylinositol anchor synthesis.
AU Leidich S D; Drapp D A; Orlean P

screen for cells blocked in [3H]inositol incorporation into protein. The gpi1 **mutant** is defective in vitro in the synthesis of N-acetylglucosaminyl phosphatidylinositol, the first intermediate in GPI synthesis, and is also **temperature-sensitive** for growth. Completion of the first step in GPI assembly is therefore required for growth of the unicellular eukaryote S. cerevisiae. GPI synthesis could therefore be exploited as a target for antifungal or antiparasitic agents.

L28 ANSWER 55 OF 67 MEDLINE
AN 94187710 MEDLINE
DN 94187710
TI NHP6A and NHP6B, which encode HMG1-like proteins, are candidates for downstream components of the **yeast** SLT2 mitogen-activated protein kinase pathway.
AU Costigan C; Kolodrubetz D; Snyder M
CS Department of Biology, Yale University, New Haven, Connecticut 06520-8103.
NC GM36494 (NIGMS)
GM45793 (NIGMS)
SO MOLECULAR AND CELLULAR BIOLOGY, (1994 Apr) 14 (4) 2391-403.
Journal code: NGY. ISSN: 0270-7306.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199406
AB The **yeast** SLK1 (BCK1) gene encodes a mitogen-activated protein kinase (MAPK) activator protein which functions upstream in a protein kinase cascade that converges on the MAPK Slt2p (Mpk1p). Dominant alleles of SLK1 have been shown to bypass the conditional lethality of a protein kinase C mutation, pkc1-delta, suggesting that Pkc1p may regulate Slk1p function. Slk1p has an important role in morphogenesis and growth control, and deletions of the SLK1 gene are lethal in a spa2-delta **mutant** background. To search for genes that interact with the SLK1-SLT2 pathway, a synthetic lethal suppression **screen** was carried out. Genes which in multiple copies suppress the synthetic lethality of slk1-1 spa2-delta were identified, and one, the NHP6A gene, has been extensively characterized. The NHP6A gene and the closely related NHP6B gene were shown previously to encode HMG1-like chromatin-associated proteins. We demonstrate here that these genes are functionally redundant and that multiple copies of either NHP6A or NHP6B suppress slk1-delta and slt2-delta. Strains from which both NHP6 genes were deleted (nhp6-delta mutants) share many phenotypes with pkc1-delta, slk1-delta, and slt2-delta mutants. nhp6-delta cells display a **temperature-sensitive** growth defect that is rescued by the addition of 1 M sorbitol to the medium, and they are **sensitive** to starvation. nhp6-delta strains also exhibit a variety of morphological and cytoskeletal defects. At the restrictive **temperature** for growth, nhp6-delta **mutant** cells contain elongated buds and enlarged necks. Many cells have patches of chitin staining on their cell surfaces, and chitin deposition is enhanced at the necks of budded cells. nhp6-delta cells display a defect in actin polarity and often accumulate large actin chunks. Genetic and phenotypic analysis indicates that NHP6A and NHP6B function downstream of SLT2. Our results indicate that the Slt2p MAPK pathway in Saccharomyces cerevisiae may mediate its function in cell growth and morphogenesis, at least in part, through high-mobility group proteins.

L28 ANSWER 56 OF 67 MEDLINE
AN 94151354 MEDLINE
DN 94151354
TI A **screen** for **yeast** mutants with defects in the dolichol-mediated pathway for N-glycosylation.
AU Roos J; Sternglanz R; Lennarz W J
CS Department of Biochemistry and Cell Biology, State University of New York at Stony Brook 11794-5215.
NC GM33184 (NIGMS)

as in higher eukaryotes, a number of the enzymes in the polyisoprenoid and glycoprotein biosynthetic pathways have not been identified. In this study, we have developed a convenient, highly **sensitive** assay that uses one of the end products of the dolichylphosphate synthetic pathway, oligosaccharide-diphosphodolichol, and a 125I-labeled peptide substrate for N-linked glycosylation to **screen** a collection of **temperature-sensitive yeast** mutants for defects in protein glycosylation. By using a combination of biochemical and genetic procedures, the defective mutants were grouped into three categories: those containing defects in dolichyl-phosphate synthesis (class 1), lipid-linked oligosaccharide assembly (class 2), or oligosaccharide transferase activity (class 3). Among the mutants identified by this **screen** were sec59 (which encodes dolichol kinase) and a **mutant** that affects the activity of the ALG1-encoded mannosyltransferase that forms dolichol-PP-(GlcNAc)2Man1. Of particular interest was a **mutant** that exhibits a **temperature-sensitive** defect in oligosaccharide transferase activity. This **mutant**, meg1 (microsomal protein essential for glycosylation 1) assembles a complete oligosaccharide chain and, therefore, is likely to be a class 3 **mutant**. We report the cloning of MEG1, the gene that rescues the oligosaccharide transferase activity defect in this **mutant**. A number of criteria distinguish this gene from previously described genes in this pathway.

L28 ANSWER 57 OF 67 MEDLINE
AN 93302762 MEDLINE
DN 93302762
TI [Stable maintenance of dicentric mini-chromosomes in CHL4 mutants in **yeast**].
Stabil'noe podderzhanie ditsentricheskikh mini-khromosom u mutanta drozhzhei po genu chl4.
AU Kuprina NIu; Krol' E S; Koriabin MIu; Bannikov V M; Kirillov A V; Zakhar'ev V M; Larionov V L
SO MOLEKULIARNAIA BIOLOGIIA, (1993 May-Jun) 27 (3) 589-607.
Journal code: NGX. ISSN: 0026-8984.
CY RUSSIA: Russian Federation
DT Journal; Article; (JOURNAL ARTICLE)
LA Russian
FS Priority Journals
EM 199309
AB Earlier we have identified the chl4-1 mutation in a **screen** for **yeast** mutants with increased loss of chromosome III and circular artificial minichromosome in mitosis. Mutation in the CHL4 gene leads to a 50-100-fold promotion in the rate of chromosome loss per cell division compared to the isogenic wild type strain. Detailed analysis of behaviour of the circular minichromosome marked by the CUP1 gene has shown that minichromosome nondisjunction (2:0 segregation) leading to an increase in the copy number of minichromosome in part of a cell population is the main reason of minichromosome instability in the **mutant**. The unique peculiarity of chl4-1 mutation is the ability of the strains carrying this mutation to stably maintain circular dicentric minichromosomes without any rearrangement during many generations. (In the wild type strains dicentric minichromosomes are extremely unstable. As a consequence of that there is a strong selection for cells harboring monocentric derivatives in a population of cells derived from a cell containing a dicentric plasmid). Introduction of the second centromere into one of the natural chromosomes (chromosomes II or III) in the chl4-1 **mutant** leads to the same dramatic consequences as that in the wild type strain (mitotic lag of cells harboring dicentric chromosomes and, as a result of that, selective pressure for cells harboring monocentric derivatives of dicentric chromosome). A genomic clone of CHL4 was isolated by complementation of the chl4-1 mutation. Nucleotide sequence analysis of CHL4 revealed a 1.4-kb open reading frame with a predicted 53-kDa protein sequence. Analyzing the sequence of the CHL4 protein we have found a region meeting the necessary requirements for the helix-turn-helix (HTH) structure. This region of the CHL4 protein has about 40% homology with the repressor of tryptophane operon (TrpR) of E. coli. A strain containing a null allele

Center, Dallas 75235..
NC GM22201 (NIGMS)
GM29935 (NIGMS)
GM31689 (NIGMS)
+
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1993 Jun 15) 90 (12) 5623-7.
Journal code: PV3. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
OS GENBANK-L15423
EM 199309
AB Chromatin becomes reorganized during mitosis each cell cycle. To identify genes potentially involved in these supramolecular events, we have used a colony-color assay to **screen temperature-sensitive** mutants of Saccharomyces cerevisiae. When a sequence that mediates attachment to the nuclear matrix in vitro was inserted into the GAL1 promoter of a lacZ fusion gene, beta-galactosidase synthesis was inhibited. This observation permitted screening for **temperature-sensitive**-inducible mutants on 5-bromo-4-chloro-3-indolyl beta-D-galactoside plates. Only 1 of 20 complementation groups of newly isolated mutants exhibited **temperature-sensitive** inducibility for the matrix association region but not for control CEN3 or STE6 inserts--a cmd1 **mutant** in which the last 7 amino acids of calmodulin were truncated by an ochre termination codon. Another **mutant** (smi1) exhibited a rare phenotype at the nonpermissive condition, which included S phase and budding arrest. We cloned and sequenced the SMI1 gene, which encodes a 57-kDa polypeptide with evolutionarily conserved epitope(s) found in mammalian cell nuclei. Thus, we provide evidence for involvement of calmodulin and another conserved protein in the in vivo binding of a matrix association region.

L28 ANSWER 59 OF 67 MEDLINE
AN 93186811 MEDLINE
DN 93186811
TI Genetic and biochemical analyses of **yeast** TATA-binding protein mutants.
AU Poon D; Knittle R A; Sabelko K A; Yamamoto T; Horikoshi M; Roeder R G; Weil P A
CS Department of Molecular Physiology and Biophysics, Vanderbilt University School of Medicine, Nashville, Tennessee 37232..
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1993 Mar 5) 268 (7) 5005-13.
Journal code: HIV. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199306
AB We have taken a combined genetic and biochemical approach to study TATA-binding protein (TBP) structure-function relationships. Using site-directed mutagenesis coupled with a **screen** for conditional lethal growth, we have isolated a number of **temperature-sensitive** TBP alleles in the region of amino acid positions 188, 189, and 190. Conditional growth is not a result of increased TBP turnover as most of the **mutant** proteins are stable in vivo as evidenced by immunoblot detection of TBP steady-state levels. DNA binding assays reveal that mutations at position 188 do not affect DNA binding activity of these mutants, even at high temperatures. Utilizing whole cell extracts which contain **mutant** TBPs in in vitro transcription experiments, we confirm that TBP is required for transcription by all three nuclear polymerases. However, certain of our TBP mutants are only compromised for RNA polymerase II transcription.

L28 ANSWER 60 OF 67 MEDLINE
AN 93078779 MEDLINE
DN 93078779
TI A mutation in the tRNA nucleotidyltransferase gene promotes stabilization of mRNAs in Saccharomyces cerevisiae.

conditional lethal mutants that affect mRNA steady-state levels. A **screen** of a collection of **temperature-sensitive** mutants identified ts352, a **mutant** that accumulated moderately stable and unstable mRNAs after a shift from 23 to 37 degrees C (M. Aebi, G. Kirchner, J.-Y. Chen, U. Vijayraghavan, A. Jacobson, N.C. Martin, and J. Abelson, J. Biol. Chem. 265:16216-16220, 1990). ts352 has a defect in the CCA1 gene, which codes for tRNA nucleotidyltransferase, the enzyme that adds 3' CCA termini to tRNAs (Aebi et al., J. Biol. Chem., 1990). In a shift to the nonpermissive **temperature**, ts352 (cca1-1) cells rapidly cease protein synthesis, reduce the rates of degradation of the CDC4, TCM1, and PAB1 mRNAs three- to fivefold, and increase the relative number of ribosomes associated with mRNAs and the overall size of polysomes. These results were analogous to those observed for cycloheximide-treated cells and are generally consistent with models that invoke a role for translational elongation in the process of mRNA turnover.

L28 ANSWER 61 OF 67 MEDLINE
AN 93024310 MEDLINE
DN 93024310
TI Translational readthrough at nonsense mutations in the HSF1 gene of Saccharomyces cerevisiae.
AU Kopczynski J B; Raff A C; Bonner J J
CS Department of Biology, Indiana University, Bloomington 47405..
SO MOLECULAR AND GENERAL GENETICS, (1992 Sep) 234 (3) 369-78.
Journal code: NGP. ISSN: 0026-8925.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199301
AB The HSF1 gene of Saccharomyces cerevisiae directs the synthesis of the heat shock transcription factor, HSF. The gene is essential; disruption mutations are lethal. Using a plasmid shuffle **screen**, we isolated mutations in the HSF1 gene after in vitro mutagenesis of plasmid DNA with hydroxylamine. From a collection of both conditional (**temperature-sensitive**) and unconditional lethal mutations, we recovered mutations that map exclusively to the 5' half of the gene. All are nonsense mutations, including conditional mutations that map 5' to the portion of the HSF1 gene that encodes the DNA-binding domain of the transcription factor. For one such mutation, we demonstrated that the nonsense mutation is subject to translational readthrough, even though there are no known nonsense suppressors in the genetic background of our strain. Our results suggest that the HSF protein is highly tolerant of amino acid changes, a conclusion that is consistent with the very low degree of evolutionary conservation among HSF proteins. Our results also suggest that translational readthrough occurs with moderate efficiency in **yeast**, particularly when the terminator codon is followed immediately by an A or C residue. This result illustrates that the inference of gene function from **mutant** phenotype depends critically upon the analysis of a true null allele, and not merely an amber or ochre allele.

L28 ANSWER 62 OF 67 MEDLINE
AN 92375083 MEDLINE
DN 92375083
TI Genetic interaction between transcription elongation factor TFIIS and RNA polymerase II.
AU Archambault J; Lacroute F; Ruet A; Friesen J D
CS Department of Genetics, Hospital for Sick Children, Toronto, Ontario, Canada..
SO MOLECULAR AND CELLULAR BIOLOGY, (1992 Sep) 12 (9) 4142-52.
Journal code: NGY. ISSN: 0270-7306.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199211
AB Little is known about the regions of RNA polymerase II (RNAPII) that are involved in the process of transcript elongation and interaction with

the seven rpo21 mutants failed to grow at elevated **temperature** underscores the im[redacted]tance of this region for the f[redacted]tional and/or structural integri[redacted]of RNAPII. We found that the 6[redacted]sensitivity of the rpo21 mutants can be suppressed by increasing the dosage of the wild-type PPR2 gene, presumably as a result of overexpression of TFIIS. These results are consistent with the proposal that in the rpo21 mutants, the formation of the RNAPII-TFIIS complex is rate limiting for the passage of the **mutant** enzyme through pausing sites. In addition to implicating a region of the largest subunit of RNAPII in the process of transcript elongation, our observations provide in vivo evidence that TFIIS is involved in transcription by RNAPII.

L28 ANSWER 63 OF 67 MEDLINE
AN 90299124 MEDLINE
DN 90299124
TI Phenotypic selection and characterization of **mutant** alleles of a eukaryotic DNA topoisomerase I.
AU Morham S G; Shuman S
CS Program in Molecular Biology, Sloan-Kettering Institute, New York, New York 10021..
NC GM-42498-01 (NIGMS)
SO GENES AND DEVELOPMENT, (1990 Apr) 4 (4) 515-24.
Journal code: FN3. ISSN: 0890-9369.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199010
AB We have developed a simple, effective genetic **screen** for **mutant** alleles of eukaryotic DNA topoisomerase I that manifest severely depressed or complete loss of enzymatic function. The **screen** is based on the extreme toxicity of vaccinia topoisomerase expression in the Escherichia coli lysogen strain BL21(DE3) and is notable for its ease in distinguishing nonsense mutations (that result in truncated proteins) from missense mutations. The power of the method is evinced by our observation that 100% of the candidate alleles identified in the **screen** were ultimately found to have single-base changes at the DNA level that result in amino acid substitutions at the protein level. By mutagenizing plasmid DNA in vitro with hydroxylamine and applying this phenotypic **screen**, we have isolated five distinct single amino acid substitution mutants, each of which shows a biochemical phenotype, that is, greater than or equal to 90% reduction in specific DNA relaxing activity of the **mutant** protein relative to wild type. The amino acids thus implicated in topoisomerase function have identical or related counterparts at homologous positions in the topoisomerases from **yeast** and man. The same genetic **screen** has been applied to the selection of **temperature-sensitive** alleles of the vaccinia topoisomerase, leading to the isolation of two additional single-hit **mutant** alleles that display a **temperature-sensitive** growth phenotype in E. coli BL21(DE3). By broadening our mutagenesis procedures, we expect to generate a comprehensive map of vaccinia topoisomerase function and primary protein structure that should have direct application to eukaryotic cellular enzymes. Our methodology should be applicable to the selection of missense and conditional **mutant** alleles in other genes whose expression in bacteria is toxic.

L28 ANSWER 64 OF 67 MEDLINE
AN 90034122 MEDLINE
DN 90034122
TI A general **screen** for **mutant** of Saccharomyces cerevisiae deficient in tRNA biosynthesis.
AU van Zyl W H; Wills N; Broach J R
CS Biology Department, Princeton University, New Jersey 08544.
NC GM34545 (NIGMS)
SO GENETICS, (1989 Sep) 123 (1) 55-68.
Journal code: FNH. ISSN: 0016-6731.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English

a variety of tRNA species. Finally, two other mutants are defective in production of tRNA from a suppressor tRNA locus, as measured by an in vitro suppression assay. The specific lesion in these strains, though, is not known. These data confirm that the **screen** does, in fact, yield a broad spectrum of mutants defective in tRNA maturation.

L28 ANSWER 65 OF 67 MEDLINE
AN 89288288 MEDLINE
DN 89288288
TI Involvement of a type 1 protein phosphatase encoded by bws1+ in fission **yeast** mitotic control.
AU Booher R; Beach D
CS Cold Spring Harbor Laboratory, New York 11724.
NC GM34607 (NIGMS)
SO CELL, (1989 Jun 16) 57 (6) 1009-16.
Journal code: CQ4. ISSN: 0092-8674.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
OS GENBANK-M27075
EM 198910
AB Fission **yeast** cdc25+ and wee1+ interact genetically with cdc2+ in the regulation of cell division, respectively as a mitotic activator and inhibitor. cdc25+ is normally essential for mitosis, but this requirement is alleviated in a loss-of-function wee1 **mutant** background. A plasmid-borne sequence, other than wee1+, that causes a cdc25ts wee1- double **mutant** to revert to a **temperature -sensitive** cdc phenotype has been isolated. The gene carried by this plasmid is called bws1+ (for bypass of wee suppression). bws1+ also bypasses the ability of alleles of cdc2 that confer a wee phenotype (cdc2w) to suppress loss-of-function cdc25 mutants. The nucleotide sequence of bws1+ shows that the predicted protein shares 81% amino acid identity with the catalytic subunit of mammalian type 1 protein phosphatase. Thus a genetic **screen** that might have yielded a protein kinase (wee1+) uncovered a phosphatase that also appears to be involved in the pathway of mitotic control.

L28 ANSWER 66 OF 67 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1997:406302 BIOSIS
DN PREV199799712505
TI The Arabidopsis CKs1At protein binds the cyclin-dependent kinases Cdc2aAT and Cdc2bAt.
AU De Veylder, Lieven; Segers, Gerda; Glab, Nathalie; Casteels, Peter; Van Montagu, Marc (1); Inze, Dirk
CS (1) Lab. Genetica, Dep. Genetics, Flanders Interuniversity Inst. Biotechnol., Univ. Gent, K.L. Ledeganckstraat 35, B-9000 Gent Belgium
SO FEBS Letters, (1997) Vol. 412, No. 3, pp. 446-452.
ISSN: 0014-5793.
DT Article
LA English
AB In Arabidopsis, two cyclin-dependent kinases (CDK), Cdc2aAt and Cdc2bAt, have been described. Here, we have used the **yeast** two-hybrid system to identify Arabidopsis proteins interacting with Cdc2aAt. Three different clones were isolated, one of which encodes a Suc1/Cks1 homologue. The functionality of the Arabidopsis Suc1/Cks1 homologue, designed Cks1At, was demonstrated by its ability to rescue the **temperature-sensitive** cdc2-L7 strain of fission **yeast** at low and intermediate expression levels. In contrast, high cks1At expression levels inhibited cell division in both **mutant** and wild-type **yeast** strains. Cks1At binds both Cdc2aAt and Cdc2bAt in vivo and in vitro. Furthermore, we demonstrate that the fission **yeast** Suc1 binds Cdc2aAt but only weakly Cdc2bAt, whereas the human CksHs1 associated exclusively with Cdc2aAt.

L28 ANSWER 67 OF 67 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1981:176789 BIOSIS
DN BA71:46781
TI RADIOMETRIC PRE **SCREEN** FOR ANTI TUMOR ACTIVITY WITH A SACCHAROMYCES-CEREVISIAE **MUTANT** STRAIN.
AU SPEEDIE M K; FIQUE D V; BLOMSTER R N
CS DEP. MED. CHEM. PHARMACOGN., SCH. PHARM., UNIV. MD., BALTIMORE, MD.

medium, time of incubation, **temperature** and size of inoculum. Known antitumor ag[redacted]s, including bleomycin, actino[redacted]in D, adriamycin and ellipticine were tested in the system and differential inhibition was observed. Vincristine showed no inhibitory effects at the concentrations tried. The sensitivity for 20% inhibition ranged from 0.8 .mu.g of adriamycin per ml to 0.14 mg of ellipticine per ml. Antifungal agents such as amphotericin B exhibited no differential inhibition. Antibacterial agents were inactive. This method may provide a rapid, **sensitive**, in vitro quantitative assay for antitumor agents which could be applied to a variety of assay needs and which can be run with facilities and equipment available in most laboratories.